Background: Transgastric cholecystectomy is a natural orifice transluminal endoscopic surgery (NOTES) procedure that has been reported in 2 nonsurvival studies. Both studies detail substantial technical limitations, with only a 33% success rate when limited to 1 gastric incision site, despite the use of a multichannel locking endoscope.

Objective: The aim of this study was to evaluate the feasibility and technical limitations of transcolonic cholecystectomy in a survival model.

Design: Animal feasibility study.

Interventions: Five pigs, under general anesthesia, were prepared with tap-water enemas, a peranal antibiotic lavage, and a Betadine rinse. A dual-channel endoscope was advanced into the peritoneum through an anterior, transcolonic incision 15 to 20 cm from the anus. After cystic duct and artery ligation, dissection of the gallbladder was achieved by using grasping and cutting instruments. After removing the gallbladder, the colonic incision was closed by using Endoloops and/or endoclips. The animals lived for 2 weeks after the procedure, then they were euthanized, and a necropsy was performed.

Results: All 5 gallbladders were successfully resected. Four of the 5 animals flourished in the postoperative period, with appropriate weight gain. In 1 animal, complete closure of the colonic incision was not possible, and it was euthanized at 48 hours for suspected peritonitis.

Conclusions: This study reports the first transcolonic organ resection and demonstrates the first successful NOTES cholecystectomy in a survival model. The transcolonic approach provided improved endoscope stability and biliary exposure compared with the transgastric route, and complete incision closure appeared critical for procedural success.

The evolution of gallbladder surgery has spanned a 300-year period. Unfortunately, most technical advances in this area have been met with skepticism. The first reported cholecystectomy was in 1709 in a dog model.1 In 1882, the procedure was performed in humans for the first time by Carl Langenbuch in Berlin.2 Langenbuch advocated cholecystectomy for the treatment of cholecystitis instead of cholecystostomy, which was the accepted practice. This new operation gave rise to heated international discussions, and controversy surrounding the procedure persisted for several decades. The next major evolutionary step in gallbladder surgery was conversion from laparotomy to laparoscopy.3 When Erich Muhe reported the first laparoscopic cholecystectomy in 1985, the German Surgical Society rejected the procedure.4 Increasing interest in laparoscopy developed only after the French gynecologist Mouret performed the procedure with 4 trocars in 1987.5 Although initially offered only to patients with uncomplicated biliary-tract disease, this procedure is now safely preformed in individuals with acute cholecystitis and choledocholithiasis.

As gallbladder surgery has evolved, flexible endoscopy has evolved in parallel. Now the next major evolutionary step in each area may bring a convergence of the 2 disciplines. In 2004, Kalloo et al6 first reported accessing the peritoneal cavity through a transgastric incision. Subsequently, our group completed a series of survival experiments by using a transgastric approach for complete systematic abdominal exploration, oophorectomy, and...
hysterectomy in the porcine model.7-9 Through a transgastric incision, the ability to identify, manipulate, and resect the gallbladder has proven to be technically challenging.10,11 To overcome the obstacles encountered through a transgastric incision, we hypothesized that a transluminal approach that provides an en face orientation to organs in the upper abdomen would allow for better visualization and scope stability. The purpose of this study was to use a novel transcolonic approach to achieve scarless natural orifice cholecystectomy with survival in a porcine model.

MATERIALS AND METHODS

Endoscopes and instruments

A standard flexible sigmoidoscope and double-channel gastroduodenoscope (GIF Q160 and GIF 2T100; Olympus Optical Co, Ltd, Tokyo, Japan) were used for each procedure. Reusable endoscopic tools used throughout the procedure included cold and hot biopsy forceps, snares, Endoloops (Olympus), prototype endoscopic scissors (Microvasive Endoscopy, Boston Scientific Corp, Natick, Mass), a hook knife, and insulated-tip and regular needle knives. Endoscopes and equipment necessary for transluminal exploration and dissection were cleaned by using high-level chemical disinfection in 2.4% glutaraldehyde (Cidex; Johnson and Johnson, Irvine, Calif) before each procedure. Disposable endoclips and Endoloops were supplied by Olympus Optical Co, Ltd, Tokyo, Japan.

Animals

Five female Yorkshire pigs that weighed 27 to 33 kg were obtained from Parson’s Farm in Hadley, Massachusetts, for use in this study. All the pigs were housed and cared for at the Animal Research at Children’s Hospital facility, Boston, Massachusetts. The study was conducted in accordance with the U.S.D.A. Animal Welfare Act, and the Animal Research Committee at Children’s Hospital approved the protocol.

The pigs were food deprived for 48 hours before surgery. The animals received preoperative cefazolin 1 g intravenously (IV). General anesthesia was induced with Telazol (4.4 mg/kg IV; Fort Dodge Animal Health, Fort Dodge, Iowa), xylazine (2.2 mg/kg IV), and atropine sulfate (0.04 mg/kg IV). After endotracheal intubation, the pigs were maintained throughout surgery on semiclosed circuit inhalation of 1% to 3% isoflurane (Cidex; Johnson and Johnson, Irvine, Calif). Two sequential 300-mL sterile-water enemas were administered, followed by endoscopic inspection with a flexible sigmoidoscope of the distal colon to 45 cm from the anus. Residual stool was removed with snares, aggressive washing, and suctioning. After removal of all particulate matter, a cefazolin suspension (1 g in 500 mL normal saline solution) was instilled endoscopically into the distal colon and the rectum. The distal colon, the rectum, and the anal orifice were prepared with both internal instillations of Betadine (Purdue Pharma LP, Stamford, Conn) and an external Betadine scrub followed by appropriate draping.

Procedure

The animals were placed in Trendelenburg’s position at the beginning of the procedure. A sterile dual-channel endoscope was introduced through the anus and advanced 15 to 20 cm from the anal verge. The colonic incision site was carefully chosen after confirming the anterior positioning by observing the internal indentation produced by palpation of the ventral abdominal wall. A needle knife was used to make a subcentimeter linear incision. Once the incision was complete, the needle knife was retracted, and the catheter was advanced through the incision into the peritoneum. By using the catheter as a guide, the endoscope was then advanced through the colonic wall into the peritoneal cavity. With the endoscope in the peritoneal cavity, the standard endoscope air pump was used to induce and maintain pneumoperitoneum. A 16-gauge catheter was placed percutaneously into the abdomen and was vented, as required, to maintain a favorable balance and to allow for optimal exposure but avoided excessive pressure that could lead to respiratory compromise or decreased venous return.

After advancing the endoscope into the peritoneal cavity, a cursory abdominal exploration was completed. From the transcolonic approach, full visualization of the upper abdominal organs, including the liver, the gallbladder, and the spleen, was possible (Fig. 1). Each lobe of the liver was then examined, and the contours were traced until the gallbladder was identified. A grasping forceps was used to pull the gallbladder away from the fossa (Fig. 2). In 3 of the pigs, the cystic duct and artery were readily exposed with this simple manipulation. In the other 2 pigs, the duct and the artery could only be identified after careful dissection of the organ from the fossa was completed. Once identified, the cystic duct and artery were ligated with endoclips (Fig. 3). Dissection of the gallbladder from the fossa then continued. A large grasping forceps

Capsule Summary

What is already known on this topic

- Endoscopic cholecystectomy has been attempted through a transgastric incision with only limited success, because of problems with biliary anatomy exposure, scope stability, and triangulation.

What this study adds to our knowledge

- Gallbladders in 5 pigs were successfully resected through an anterior, transcolonic incision 15 to 20 cm from the anus.
was used to pull the gallbladder away from the fossa, and numerous tools were used to separate the fibrotic layers of attachment (Fig. 4). The tools used in this endeavor included a hot biopsy forceps, a snare tip, a hook knife, a prototype endoscopic scissors (Microvasive), and an insulated-tip needle knife. Once the majority of tissue attachments connecting the gallbladder and the fossa were severed, complete removal was achieved with snare cautery (Fig. 5). Once resected, the gallbladder was retrieved from the abdominal cavity and removed through the colotomy in 1 piece.

After removal of the organ, the resection site was washed and inspected for residual defects, bleeding, and bile leakage. Adjacent organs were evaluated for evidence of laceration, perforation, and hemorrhage. When present, defects were closed with endoclips, and hemostasis was accomplished with electrocautery. The pneumoperitoneum was then evacuated with suction, and the endoscope was retracted into the distal colon.

Finally, the colonic exit site was addressed. In 1 pig, a single Endoloop was used to close the colonic incision. In the other 4 pigs, 3 to 8 endoclips (Fig. 6) were used to achieve closure. The incision edges were secured together by using 1 or both devices. After closure of the colonic incision, residual air was evacuated from the peritoneum via the external percutaneous catheter, and the catheter was removed. The surgical techniques described in this section are further illustrated in Video 1 (available online at www.giejournal.org).

**Postoperative care**

After surgery, all the pigs were extubated, recovered, and then transferred to housing pens. They were given a topical 25 mg fentanyl patch for analgesia, and enrofloxacin 250 mg was administered twice daily by mouth for 3 days. A regular diet was resumed within hours of surgery. All the pigs were closely monitored twice daily by the veterinary staff for signs of distress, behavior changes, or changes in feeding habits.

**Necropsy and tissue examination**

When possible, the pigs were kept alive for 2 weeks before necropsy. The peritoneal cavity was examined for evidence of infection, bleeding, perforation, or adhesions. Peritoneal biopsy specimens were obtained, and the liver, including the gallbladder fossa, and the colonic incision site were harvested for gross and microscopic histopathologic examination. All specimens were fixed initially in 10% buffered formalin until tissue processing. At the time of
processing, tissue sections were obtained from all organs, randomly, and from grossly identifiable areas of pathology. Specimens were sectioned at 7-μ intervals and stained with H&E for microscope examination. Slides were reviewed by 1 gastrointestinal pathologist (R.D.O.) in a blinded fashion for a variety of inflammatory tissue reactions.

RESULTS

The abdomen and the pelvis were successfully entered through a transcolonic incision in all 5 animals. The liver, the gallbladder, and the spleen were readily identified in all cases. A complete gallbladder resection, with ligation of the cystic duct and artery, was completed in all 5 pigs. The common bile duct was not identified in any of the pigs. The average time from entrance into the peritoneal cavity to removal of the gallbladder from the anal orifice was 68 minutes (range, 42-90 minutes). The total time of the entire procedure ranged from 70 to 165 minutes, with a mean of 115 minutes. The time for the procedure improved with experience. In all cases, the gallbladder was removed in 1 piece. By microscopy, the gallbladder in all 5 pigs was histologically within normal limits, with no evidence of perforation.

Four of the 5 animals flourished in the postoperative period, with appropriate weight gain, feeding, and activity patterns. At the time of necropsy, the contents of the peritoneum of all 4 pigs appeared pink and healthy, with no signs of infection, bleeding, bile staining, or organ injury. The gallbladder fossa appeared fibrosed (Fig. 7). Residual organ tissue was not seen. The colonic incision site appeared closed and fully healed from the luminal aspect. However, external adhesions were demonstrated in 3 of the 4 pigs and were confirmed by microscopic examination of the sections. In 2 pigs, salpingocolonic attachments were observed. In a third pig, colovesical attachments were present. Microscopic evaluation of the colonic incision site revealed ulceration and necrosis. Submucosal and/or serosal microabscesses were appreciated in all pigs, and necrotizing granulomas were seen in 1 pig. Microscopic evaluation of peritoneal biopsy specimens in these animals was within normal limits.

In 1 of the pigs, complete closure of the colonic incision site was not possible, and a 4-mm residual defect remained at the conclusion of the surgery. The pig survived for 48 hours but then was euthanized because of concerns of peritonitis. Necropsy and histologic findings confirmed acute peritonitis, with seepage of bowel contents from the colonic perforation.

DISCUSSION

This is the first report of transcolonic endoscopic cholecystectomy in a porcine model. Since Langenbuch
performed the first successful human cholecystectomy in 1882, surgeons have strived to minimize complication rates by observing careful dissection techniques. Over the past 20 years, resecting the gallbladder has changed from an open approach via a Kochner incision to a laparoscopic approach via 3 or 4 trocars. The surgical steps of dissection, however, did not differ much between the 2 approaches. Novel approaches to cholecystectomy should mimic classical steps of dissection. The dissection could take a Calot’s triangle–first or a fundus–first approach. The essential steps of cholecystectomy included exposure of the Calot’s triangle, dissection to expose the cystic duct and artery and avoiding damage to the common bile duct and the common hepatic duct, and dissection of the gallbladder from the liver bed. The knowledge of these essential steps in cholecystectomy served as a basis for our procedure.

Thus far, endoluminal studies have dealt primarily with the transgastric approach. In 2004, Kalloo et al published the first study to describe the transgastric method in a porcine model. In 2005, our research group showed that identification of most intra-abdominal organs is possible with this approach, and resection of the ovaries and uterus is technically feasible in a survival setting. Surprisingly, the gallbladder was not one of the organs that was consistently visualized, and our group could only identify the gallbladder in 55.6% of cases when using a single gastric incision.

Other groups had limited success in identifying and removing the gallbladder when using multiple endoscopes or prototype scopes via a transgastric approach. For instance, Swanstrom et al reported transgastric cholecystectomy, with 1 gastric perforation, when using a multichannel locking endoscope. When using Shapelock technology (USGI Medical, San Clemente, Calif), the Swanstrom team could operate from a stable platform in the right upper quadrant. A resection was done in the retroflexed position, with the body of the prototype endoscope in a locked position, which held excess liver tissue away from the surgical field. Despite the added stability afforded by the locking mechanism, the procedure was successful in only 1 of 3 animals because of visualization problems encountered after the onset of bleeding and gallbladder perforation because of limitations in control of dissection tools. In 2005, Swain’s group was successful in identifying the gallbladder and transgastric cholecystectomy by using laparoscopic assistance, a dual-channel instrument, or 2 endoscopes. Use of 2 endoscopes improved visualization and triangulation; however, insertion of the second endoscope resulted in friction between the 2 instruments and likely enlarged the gastric incision. A transabdominal forceps again improved triangulation but introduced the inherent drawbacks of an extra incision. In these nonsurvival procedures, the main problem cited by the investigators was insufficient exposure of the biliary anatomy. We felt that an approach from the inferior aspect of the peritoneal cavity through a colonic incision may provide improved exposure and better scope control and stability.

In this first report of transcolonic organ resection, certain observations are important. The colonic incision was created with a needle knife and pressure from the endoscope, unlike transgastric incisions, which require balloon dilation. The pigs were positioned head down so that gravity would assist in keeping adjacent structures away from the colonic exit site. At necropsy, nearby structures showed no signs of incidental damage. In future studies, the creation of a pneumoperitoneum with CO2 insufflation before the transluminal incision may have a role in minimizing the risk of adjacent organ damage; US could also be of value in initial studies to confirm appropriate anterior positioning and location of nearby structures. The ease with which the gallbladder could be identified and isolated from this approach was a definite asset. The biliary structures were directly approached with the endoscope, unlike in the transgastric approach, where the endoscope was in a retroflexed position to access these structures. In retroflexion, forward force exerted on the insertion tube of the endoscope resulted in paradoxical motion and thus movement away from the operative site. With the en face orientation from the transcolonic incision, we were able to operate with improved stability and greater control over the endoscope and the channel instruments.

In humans, the dissection of Calot’s triangle can be done safely, starting from Hartmann’s pouch and moving toward the cystic duct. This is particularly important in acute cases, when anatomical landmarks are difficult to find. In this procedure, the same protocol was followed, and locating the cystic duct and artery was straightforward; however, the common bile duct was not identified. Because of the potential for variability of the anatomical
landmarks and distortion during acute cases, confirmation of the biliary tree is essential. For future studies, intraoperative cholangiograms may be useful to confirm anatomy before cystic-duct ligation. To assist in dissection and visualization of the common bile duct, improvements in current tools for triangulation and liver retraction are needed.

The complication encountered in this series was not related to organ resection but rather to a problem with the colonic incision closure. In a previous series, by our laboratory, that evaluated peroral endoscopic partial hysterectomy, a near identical complication occurred when the transgastric incision was incompletely closed. In all of our transluminal experiments, closing the transluminal incision site has been a cumbersome task, but experience has taught us that we cannot tolerate any postprocedure leakage from the incision site. Closing the colonic incision presents just as difficult a challenge as the transgastric incision. During organ resection, the original incision dilates because of the constant movement of the endoscope. Furthermore, removal of the gallbladder through the colon results in additional dilatation of the colotomy. It is obvious that endoclips and Endoloops are primarily designed for achieving hemostasis and are suboptimal for assuring complete closure of these transluminal defects. The presence of adhesions at the time of necropsy reinforces the idea that closure is inadequate. A device that provides efficient and consistent surgical closure will be of critical importance.

The fact that peritoneal infection was not encountered when the colonic incision was appropriately closed was reassuring. However, the episode of supplicative peritonitis in this series reemphasizes the potential for infection with breaches in the luminal integrity. Strict sterility during this type of procedure, as in all surgical procedures, would be ideal. However, with current technology, only high-level chemical disinfection of our tools and antibiotic and Betadine lavage of the luminal surface is possible. Before human application, a sterile conduit capable of preventing spillage of luminal contents into the peritoneum must be developed.

Transcolonic organ resection is far from translation to humans, and it is unclear at present how valuable transluminal procedures will be when compared with laparoscopic or open approaches. Although the benefits of natural orifice transluminal endoscopic surgery (NOTES) cholecystectomy may seem minimally incremental when compared with traditional laparoscopic methods, the application of the approach to other procedures, eg, bariatric surgery, may provide significant advantages over current surgical procedures. The future of this field will be dictated by the ability of investigators and inventors to develop the tools and methods necessary to ensure safety, effectiveness, and efficiency of these procedures. Regardless of the final adoption of specific NOTES procedures, the techniques and devices developed for advance-

ment of the field have potential to greatly enrich traditional endoscopy and laparoscopy.

Conclusions

This study demonstrates the technical feasibility of transcolonic organ resection and represents the first successful transluminal endoscopic cholecystectomy in a survival model. As research in transluminal surgery continues, this novel approach may represent a possible route for minimally invasive surgery in the abdomen and the pelvis.

ACKNOWLEDGMENT

We thank Jerry S. Trier, MD, Department of Gastroenterology and Hepatology, Brigham and Women’s Hospital, Boston, Massachusetts, for his critical review of the manuscript.

DISCLOSURE

None of the authors have commercial associations that might be a conflict of interest in relation to this article.

Disposable endoclips and Endoloops were supplied by Olympus Optical Co, Ltd, Tokyo, Japan.

REFERENCES


Received May 5, 2006. Accepted June 20, 2006.

Current affiliations: Division of Gastroenterology (Dr Pai, Dr Fong, Ms Bundga, and Dr Thompson), Division of Pathology (Dr Odze), Brigham and Women's Hospital, Division of Surgery, Massachusetts General Hospital (Dr Rattner), Harvard Medical School, Boston, Massachusetts, USA.

Reprint requests: Christopher C. Thompson, MD, MSc, Brigham and Women's Hospital, Division of Gastroenterology, 75 Francis St, Boston, MA 02115.