

Experimental studies of Peroral Transgastric Abdominal Surgery

C. Feretis¹, D. Kalantzopoulos¹, P. Koulouris¹, C. Kolettas¹, S. Chandakas², M. Sideris³, A. Papalois³

SUMMARY

Background: Recent studies are testing the feasibility of an incisionless endoscopic per-oral approach to the peritoneal cavity in experimental animals. Herein we present our results of peroral peritoneoscopy, liver biopsy, cholecystectomy, fallopian tube and uterus excision, in a porcine model to determine the technical feasibility and safety of Peroral Transgastric Procedures. **Methods:** The procedures were performed on ten 28-50 Kgr anaesthetised pigs by using sterilized double channel endoscope and catheters. The gastric cavity was irrigated with antibiotic solution and access to the peritoneal cavity was gained after stomach wall incision with needle knife electrocautery. **Peritoneoscopy (10 pigs), liver biopsy (1 pig), cholecystectomy (6 pigs) fallopian tube excision (one pig) and Hysterectomy (1 pig) were carried out. Four acute and six survival experiments were performed. Results:** All procedures were accomplished successfully. Easily handled complications occurred in two animals. The feasibility of the peroral approach was demonstrated in all acute experiments. In the survival experiments all pigs recovered and thrived during the following four to six weeks. **Conclusion:** Evidence is given that per-oral transgastric surgery is technically feasible and safe in a porcine model. The method has potential to become an alternative to laparoscopy. Further evaluation in larger series is required.

cavity is currently being tested¹⁻⁹ for the efficacy and safety of flexible endoscopic intraabdominal diagnostic and therapeutic procedures. The transgastric route may be proved advantageous for patients by avoiding abdominal wall incisions and thus further minimizing the invasiveness of surgery.

The present pilot study in 10 pigs was conducted to assess the technical feasibility and the safety of diagnostic peritoneoscopy, liver biopsy, cholecystectomy, fallopian tube excision and hysterectomy in a porcine model with long term survival.

MATERIALS AND METHODS

The study was approved by the Ethical Committee of IASO General Hospital, ELPEN laboratories and the veterinary authorities of East Attica (Act P.D 160, 1991). Transgastric abdominal procedures were carried out in ten 28-50 Kgr pigs under general anaesthesia by endotracheal intubation.

One acute experiment was performed where four pigs underwent Peritoneoscopy (4/4), Liver biopsy (1/4), Cholecystectomy (2/4) and were immediately euthanized. Subsequently six pigs underwent Peritoneoscopy (6/6), Cholecystectomy (4/6), Fallopian Tube excision (1/6) and Hysterectomy (1/6) and were followed for four to six weeks after surgery before euthanasia.

Pig preparation: Animals were fasted for 24h before operation. All procedures were performed with animals under general anesthesia. After premedication with ketamine 15 mg / kg i.m. and midazolam 0,5 mg / Kg i.m., the animals were placed on the operating table and two iv lines were placed (ear vessels). They were intubated with a number 7.0 or 7.5 tracheal tube and ventilated mechanically (15 ml / Kg and 18 – 20 breaths per minute). The inspired oxygen concentration was 40 – 45 (Fractional inspired oxygen - FiO₂): 0.40 – 0.45).

INTRODUCTION

The per oral transgastric approach to the peritoneal

¹Department of Therapeutic Endoscopy, Iaso General Hospital Athens Greece, ²Department of Minimal Access Gynaecological Surgery, Iaso Hospital Athens Greece, ³Experimental - Research Unit ELPEN Pharma

Author for correspondence:

P. Koulouris M.D., 264 Mesogion Av.,
Holargos 15562 Athens Greece,
Tel - FAX: 2106502966, e-mail:chrisferetis@gmail.com

The induction of anesthesia was achieved with bolus iv injection of propofol 3 mg / Kg, pancuronium 0.15 mg/ Kg and fentanyl 17.5 µg/Kg. Anesthesia was maintained by iv administration of propofol 0.15 mg / Kg, pancuronium 0.07 mg /Kg bolus every 20 min and fentanyl 15 µg / Kg/ h.

Intraoperative monitoring included electrocardiography, pulse oxymetry and noninvasive measurement of arterial blood pressure. Normal saline was given as fluid replacement therapy during the procedure. Neostigmine 1 – 2 mg and atropine 0.5 mg were used for reversal of the neuromuscular blockade after the operation was over. The oral cavity of the pigs was disinfected with a solution of povidone iodine 1% and their oesophagus and stomach were thoroughly cleaned by using 1 lit of sterilised water injected through the working channel of a disinfected sigmoidoscope (Olympus CF-140S) in order to remove any food debris from the gastric cavity.

After removal of the first scope, a sterilised forward viewing double channel endoscope (Olympus GIF 2T160) was inserted into the stomach and irrigation of the gastric cavity with 1 lit of colistine solution followed.

SURGICAL TECHNIQUES

Gastric wall incision: The anterior stomach wall was incised with a needle knife (Microknife XL, Boston Scientific) by using a blended current (**fig.1**). When the needle was felt to penetrate the gastric wall the electro-surgical current was switched off, the needle was withdrawn and the catheter was advanced into the peritoneal cavity under hydrophilic 0,35 wire guidance (Jagwire, Boston Scientific). The needle knife catheter was removed and over the wire through the scope a 15mm dilatating balloon (CRE Wireguided, Boston Scientific) was used to enlarge the initial incision up to 12-15mm (**fig.2**). The endoscope was then passed and advanced into the peritoneal cavity that was insufflated with CO₂.

Peritoneoscopy: After sufficient pneumoperitoneum, the parietal peritoneum of the anterior abdominal wall, the hepatic lobes, the spleen, the coils of the small intestine, the cecum and the spiral (large) colon were clearly viewed. The urinary bladder, both ureteres running under the parietal peritoneum of the abdominal wall and the fallopian tubes, together with the ovaries and uterus were also visualised (**fig.3**). The gallbladder fundus and body were viewed between the hepatic lobes. A combination of pushing and traction forces on the gallbladder applied by flexible catheters inserted through the two channels of the scope, resulted in adequate exposure of

the gallbladder neck and cystic duct.

Liver biopsy: After a thorough examination of the peritoneal cavity, the liver edge was grasped and stabilized with endoscopic forceps (FG-49L-1, Olympus) inserted through the first working channel of the scope. Through the second larger channel hot biopsy forceps (FD-1L-1, Olympus) was used to obtain a sample of liver tissue. An additional liver tissue sample was taken by using a Trucut (Quick-Core, Wilson Cook) catheter that was embedded deeply in the liver parenchyma (**fig.4**).

Cholecystectomy: Manipulation of the fundus and body of the gallbladder through alternate grasping of its wall with two forceps (**fig. 5**) resulted in efficient exposure of cystic duct that was then ligated by using rotatable clipping devices (Long clips, Olympus). The duct was transected between the clips with a needle knife (Microknife XL, Boston Scientific) and electro-surgical current (**fig. 6**).

Separation of the gallbladder from its liver bed was carried out by combining sharp dissection with a needle knife and blunt dissection with the metal tip of a Dormia catheter (FGV411G, Olympus) by using a blended current of 20J cautery and 30J cut (**fig. 7**).

When all attachments with the liver were severed, the scope together with the grasped gallbladder was withdrawn into the gastric lumen. The gallbladder was left free in the stomach and was removed through the oesophagus and mouth only after closing the gastric incision.

Transgastric Fallopian tube excision: After entering the peritoneal cavity the scope was advanced into the pelvis. The left uterine tube was visualised and its medial portion was grasped with forceps (FG-49L-1, Olympus) through an open endoloop (MAJ-254, Olympus). Ligation was accomplished with one loop (**fig. 8**). The ligated segment was excised by using a needle knife catheter and blended current (**fig. 9**) grasped with a snare and withdrawn into the stomach. The transected tube was removed through the oesophagus and mouth.

Hysterectomy: The uterus was grasped with forceps and both uterine vessels were exposed and clipped (**fig. 10**). The uterus was excised with a needle knife catheter (**fig.11**), withdrawn into the stomach and removed through the oesophagus.

Closure of the gastric wall incision: In the acute experiments the gastric incision was sealed with an omentum patch pulled into the stomach and fixed to the edges of the gastric opening (**fig.12**) by haemostatic clips (Long clips, Olympus).



Fig.1: Gastric wall incision

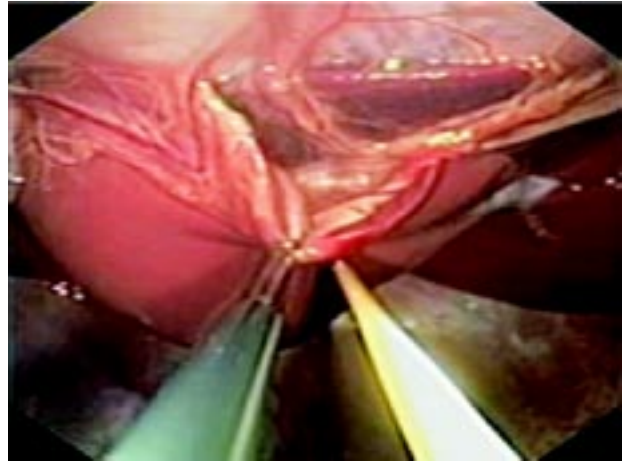


Fig.4: Liver biopsy



Fig.2: Dilatation of the opening

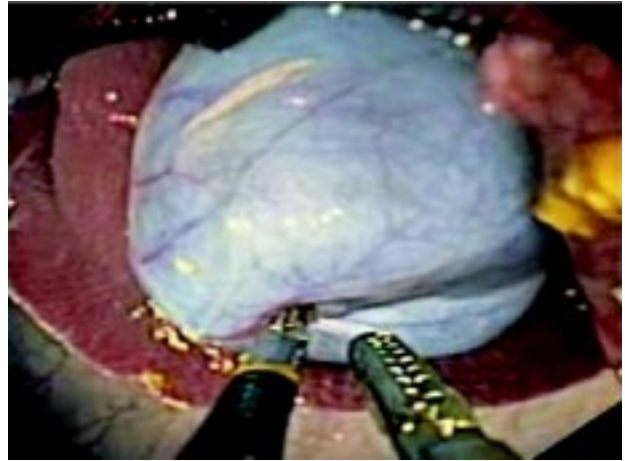


Fig.5: Manipulation of the gallbladder



Fig.3: Peritoneoscopy



Fig.6: Cystic duct transection



Fig.7: Gallbladder detachment

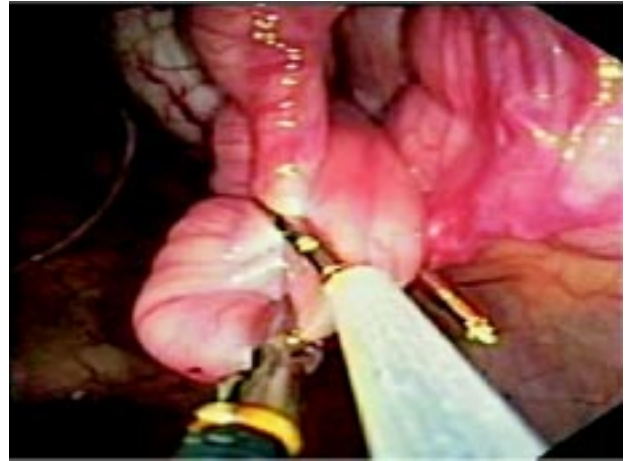


Fig.10: Clipping of the uterine vessels

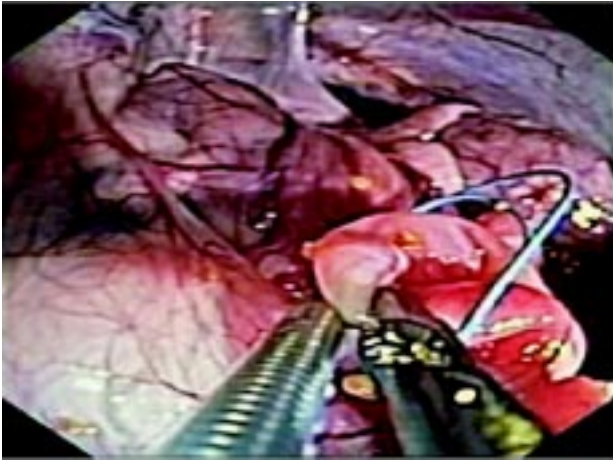


Fig.8: Fallopian tube ligation



Fig.11: Uterus excision



Fig.9: Fallopian tube excision

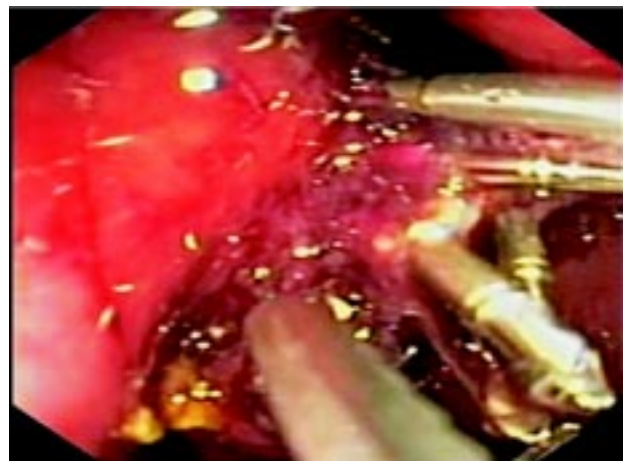


Fig.12: Omentum patch fixation

In the survival experiments the edges of the gastric opening were approximated with a long limb grasping forceps inserted through one channel of the scope.

A clipping device (Long clips, Olympus – Resolution clips, Boston Scientific) inserted through the second channel was used to apply a series of 8-10 clips to close the opening (**fig.13**). Criterion for safe closure was unhampered gastric dilatation induced by insufflation of CO₂ through the scope.

RESULTS

Acute experiments: All gastric incisions were accomplished without complications. Inadvertent entrance to the Peritoneal Cavity through the lesser sack was observed in one animal. Bleeding or injury to internal organs did not occur. The abdomen was easily distended with CO₂ insufflated through the scope. The approach of internal organs was a demanding step that was carried out successfully in all animals by combining torquing and retroflexing manoeuvres together with anchoring of the scope to the targeted area with grasping forceps. The exposure of the cystic duct required high skilled manoeuvres but was efficient in all animals. The visualisation of pelvic anatomy was satisfactory and identification of the uterus, fallopian tubes and ovaries was facilitated by reverse Trendelenburg position. Liver biopsy was conducted uneventfully and the obtained tissue samples proved sufficient to provide a reliable histological diagnosis. In two animals that were subjected to cholecystectomy the gallbladder fundus was easily identified. The exposure of the cystic duct and artery was more difficult due to the pig hepatic lobes covering the area. Ligation



Fig.13: Clipping of the gastric opening

and incision of the cystic duct and artery by a rotatable clipping device a needle knife catheter was possible in both animals without bile duct injuries. Gallbladder wall perforation induced from the grasping forceps occurred in one animal and it was managed by clip application. Dissection of the gallbladder of its liver bed was complicated by bleeding in one animal and was controlled by applying coagulation through hot biopsy forceps. The time required in the first and second cholecystectomy was 3.5 and 2.5 hours respectively.

Survival experiments: There were two complications during gastric wall incision and entrance into the peritoneal cavity. In one animal bleeding from the gastric puncture site occurred and was controlled by clip application. In a second animal a small perforation of the gallbladder was discovered during the following procedure of cholecystectomy. Inadvertent entrance to the peritoneal cavity through the lesser sac was recorded in a third animal. Four consecutive peritoneoscopies were followed by successfully accomplished cholecystectomies without any untoward effect. Abdominal pelvis exploration with fallopian tube excision was greatly facilitated by positioning the animal in a reverse Trendelenburg position. Appliance of a ligating loop and safe severance of the tube was an easy task. Procedure related complications were not encountered. Uterus visualisation, ligation of the feeding vessels and resection was performed without any complication. All pigs recovered uneventfully and tolerated a regular diet within 24 h after the procedures. During a follow up period of 4-6 weeks there were heart and thriving. No clinical signs of either bleeding or infection were observed.

DISCUSSION

The use of flexible endoscopes passing through the gastric wall into the peritoneal cavity and the performance of various intra-abdominal interventions is currently being tested as an alternate that may further reduce the invasiveness of surgery by avoiding skin incisions.

The feasibility of both diagnostic peritoneoscopy and intraabdominal surgery including liver biopsy, cholecystectomy and fallopian tube ligation was tested in the present animal study. In all five pigs there were a number of common difficulties met at each step of oral transgastric approach and surgery.

Preparation of the pig stomach and infectionless entry of the endoscope into the peritoneal cavity proved to be a difficult and costly task. It required multiple irrigations of the stomach with antibiotic solutions via a disinfectant forward viewing endoscope. After a thorough

cleaning of the gastric cavity a second sterilized forward viewing double channel endoscope was necessary to secure infectionless entry to the peritoneal cavity and minimize the risk of intraabdominal infection.

Incision of the anterior stomach wall and intraperitoneal insertion of the endoscope proved to be a relatively easy step and was facilitated by pushing and pressing the endoscope against the dilating balloon catheter. It was important to choose the most appropriate site for gastrotomy on the border of the body and antrum of the anterior wall, otherwise the lesser sac may have been inadvertently entered.

Insufflation of CO₂ through the endoscope resulted in adequate pneumoperitoneum- permitting abdominal exploration, but overinflation was a common problem that had to be faced by aspiration.

The most devastating and time consuming problem with transgastric procedures was the lack of endoscope support limiting its manoeuvrability within the peritoneal cavity. Apart from the flexible nature of the scope, the above mentioned difficulties were intensified by the mobility of the stomach and the obvious absence of any support from the abdominal wall. These limitations lead to notable difficulties in approaching the targeted organs. Superimposed restrictions were added by the noted reverse movement of the usually retroflexed endoscope away from its target when a forward pushing force was exerted.

Grasping of targeted tissues with commercially available endoscopic catheters was satisfactory for liver, gallbladder and fallopian tubes, although retraction and pushing proved troublesome for the gallbladder. Furthermore the use of a scope with two parallel running working channels creates a serious obstacle for applying simultaneous diverting and/or converting movements of flexible instruments.

Closure of the gastrotomy incision, a crucial step for the safety of transgastric approach was proved difficult by using the available clipping devices. Plugging of the hole with omentum fixed onto the incision edges reported in both experimental animals¹⁰ and human case studies,¹¹ facilitated the final approximation of wound edges in our hands. In this connection, the forthcoming release of prototype giant clips (Olympus) and/or endoscopic suturing device (Eagle claw, Olympus) is expected to eliminate this problem. At present high skills and time consuming manoeuvres are required for safe gastric incision closure.

Although the present study provides evidence for the

feasibility of peroral transgastric surgery in the porcine model, crucial technical innovations and extensive animal survival studies are required to evaluate the merits of incisionless surgery.

REFERENCES

1. Kalloo AN, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevov SV. Flexible transgastric peritoneoscopy a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. *Gastrointestinal Endoscopy* 2004;60:114-117.
2. Park PO, Bergstrom M, Ikeda K, Fritscher-Ravens A, Swain P. Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis. *Gastrointestinal Endoscopy* 2005;61:601-606.
3. Kantsevov SV, Jagannath SB, Niiyama H, Chung SS, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Magee CA, Vaughn CA, Barlow D, Shimonaka H, Kalloo AN. Endoscopic gastrojejunostomy with survival in a porcine model. *Gastrointestinal Endoscopy* 2005;62:287-292.
4. Jagannath SB, Kantsevov SV, Vaughn CA, Chung SS, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Scorpio DG, Magee CA, Pipitone LJ, Kalloo AN. Peroral transgastric endoscopic ligation of fallopian tubes with long-term survival in a porcine model. *Gastrointestinal Endoscopy* 2005;61:449-453.
5. Swanstrom LL, Kozarek R, Pasricha PJ, Gross S, Birkett D, Park PO, Saadat V, Ewers R, Swain P. Development of a new access device for transgastric surgery. *J Gastrointest Surg.* 2005;9:1129-1137.
6. Wagh MS, Merrifield BF, Thompson CC. Endoscopic transgastric abdominal exploration and organ resection: initial experience in a porcine model. *Clin Gastroenterol Hepatol.*2005;3:892-896.
7. Rattner D., Kalloo AN. and the SAGES/ASGE ASGE/SAGES Working Group on Natural Orifice Transluminal Endoscopic Surgery. *Surg. Endosc* 2006;20:329-333.
8. Bergstrom M, Ikeda K, Swain P, Park P. Transgastric endoscopic splenectomy Is it possible? *Surg Endosc.* 2006 Jan 21;
9. Kantsevov SV, Hu B, Jagannath SB, Vaughn CA, Beitler DM, Chung SS, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Magee CA, Pipitone LJ, Talamini MA, Kalloo AN. Transgastric anastomosis by using flexible endoscopy in a porcine model (with video). *Gastrointest Endosc.* 2006;63:307-312.
10. Hashiba K, Carvalho AM, Diniz G Jr, Barbosa de Aridade N, Guedes CA, Siqueira Filho L, Lima CA, Coehlo HE, de Oliveira RA. Experimental endoscopic repair of gastric perforations with an omental patch and clips. *Gastrointestinal Endoscopy* 2001;54:500-504.
11. Tsunada S, Ogata S, Ohyama T, Ootani H, Oda K, Kikkawa A, Ootani A, Sakata H, Iwakiri R, Fujimoto K. Endoscopic closure of perforations caused by EMR in the stomach by application of metallic clips. *Gastrointestinal Endoscopy* 2003;57:948-951.