

Natural orifice transluminal endoscopic surgery in humans: feasibility and safety of transgastric closure using the OTSC system

Richard Magdeburg¹ · Georg Kaehler¹

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Abstract

Background NOTES is a technique in which an operation is performed within the body without a skin incision by using a natural body orifice to provide access. The principal challenge of transgastric NOTES procedures is still the feasibility and safety of access closure. Currently, there are very limited data regarding the closure of transgastric NOTES in humans, and the standard method and device for closure has not been defined. Herein, we evaluate the feasibility and safety of gastric closure after NOTES procedures in humans with the over-the-scope clip (OTSC).

Methods Review of collected data of patients underwent transgastric NOTES in prospective clinical studies between April 2010 and March 2014 focused on the gastric closure with the OTSC.

Results A total of 43 patients underwent transgastric NOTES: 36 patients with an acute appendicitis, six patients with a prophylactic bilateral salpingo-oophorectomy, and one patient with uterus myomatosis. In all 43 cases, the incision of the gastric wall and the endoscopic access to the abdominal cavity succeeded without any difficulty. After performing transgastric procedures, it was possible to close the access by OTSC in all cases. There were all in all three adverse events: one major (Clavien–Dindo Grade III) and two minor (Clavien–Dindo Grades I and II).

Conclusion Even if we could show for the first time in more than 40 consecutive patients that there is a safe approach for closing the transgastric access, it is absolutely necessary that further investigation in clinical settings has to be done to establish clear indications and guidelines for the use of transgastric NOTES.

Keywords NOTES · OTSC · Transgastric · Closure

Advantages of laparoscopic surgery in comparison with open surgery are well established [1, 2]. One focus of this evolution has been to make surgery less invasive. Natural orifice transluminal endoscopic surgery (NOTES) has been described as the next surgical frontier with the objective of incision-free abdominal surgery. NOTES is a technique in which an operation is performed within the body without a skin incision by using a natural body orifice to provide access [3]. In NOTES, surgical procedures are performed with an endoscope passed through a natural orifice such as the esophagus, stomach, rectum, colon, vagina, or urethra [4]. To achieve this goal, surgeons are either decreasing the number of trocars placed through the abdominal wall or eliminating them completely [5]. However, the principal challenge of NOTES procedures is still the feasibility and safety of gastric closure. Obtaining reliable closure of access points at the completion of a NOTES procedure is currently the most significant limitation and one of the main factors that will determine the future of NOTES in clinical use [4, 6]. There are several closure techniques being tested in experimental settings today. Ideal closure should be rapid, reproducible, and safe. A potential device that can achieve full-thickness gastrointestinal closure is the over-the-scope clip (OTSC) (Ovesco Endoscopy, Tübingen, Germany) [7]. Primarily, the OTSC system was

✉ Richard Magdeburg
richard.magdeburg@umm.de

¹ Department of Surgery, Medical Faculty Mannheim, University Medical Centre Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany

developed for treatment of bleeding ulcers and for closure of iatrogenic perforations in the gastrointestinal tract. The OTSC system has been studied extensively, and its use seems to provide an easy, safe, and reliable way to close gastrointestinal perforations and has even shown favorable results with regard to acute closure strength compared with surgical closures [8]. However, reliability, safety, and efficacy of this tool have yet to be fully characterized in a clinical setting [4]. Even if the main postulation of the medical society at the beginning of NOTES was the safety of access closure, there are currently very limited data regarding the closure of transgastric NOTES procedures in humans. We first present a clinical series of 43 consecutive patients underwent transgastric NOTES procedures in the abdominal cavity. Indications have been acute appendicitis (36), bilateral salpingo-oophorectomy for the presence of BRCA1 or BRCA2 mutations (6), and hysterectomy for uterus myomatosis (1). The gastric access was closed with the OTSC system in all cases. The focus of this study is the feasibility and safety of gastric closure.

Materials and methods

All patients have been treated in prospective clinical studies with approval by the independent ethics committee (IEC) of the University of Heidelberg in Germany. A special patient insurance was taken out. The studies transgastric appendectomy and transgastric salpingo-oophorectomy were prospectively registered in the German registry for clinical studies (Deutsches Register für Klinische Studien; DRKS-ID: DRKS00000398 and DRKS00003582).

All patients received oral lavage with octenidine HCL (Octenidin Mundspüllösung, Schülke & Mayr GmbH, 22840, Norderstedt, Germany). After establishing a standard general anesthesia, the patient was positioned on a vacuum mattress to facilitate extreme positioning during the procedure. Before the procedure, a single-shot antibiotic therapy, consisting of 500 mg ceftriaxone and 500 mg metronidazole, was administered. The procedure was done with a double-channel therapeutic gastroscope (Karl Storz PV-TG 2) together with an endoscopy system (light source Xenon 100, video processor Telecam SL II, Documentation system Aida control, Karl Storz Endoskope, Tuttlingen, Germany) which was sterilized with ethylene oxide and provided in a sterile box. One of the channels is connected to a CO₂ insufflator (Karl Storz Thermoflator, Karl Storz Endoskope, Tuttlingen, Germany, flow: 6 l/min CO₂; pressure: 15 mmHg), and the other is used for instrumentation.

The transgastric procedure was performed as previously described by our group [5, 9]. All procedures were performed, respectively, by one of two endoscopically experienced surgeons after expanded training in animals. The

procedure began with routine gastroscopy to exclude abnormalities in the esophagus and stomach. After identification of the middle third of the anterior wall of the corpus by “fingertip trial” from the left epigastrium (similar to endoscopic percutaneous gastrotomy application), the puncture region was marked with five coagulation marks. This was done to locate the insertion, in case the endoscope had to be removed during the operation. Via gastroscope, the gastric wall was punctured with a high-frequency electro-surgical needle knife (Needle Papillotome, MTW Endoskopie, Wesel, Germany; ICC 200 high-frequency generator; Erbe Elektromedizin, Tübingen, Germany), and a 450-cm guide wire (Jagwire; Boston Scientific, Ratingen, Germany) was inserted. After removal of the needle knife, a dilation balloon (Rigiflex 18–19–20 mm; Boston Scientific) was introduced and the hole in the gastric wall was dilated. As the balloon was deflating, the gastroscope was advanced into the peritoneum, and a pneumoperitoneum with standard laparoscopy pressure of 12 mm Hg was established and maintained with an automatic insufflator (Laparoflator, Karl Storz).

For appendectomy after diagnostic exploration of the abdominal cavity, a single 5-mm trocar was inserted in the umbilicus under endoscopic vision. With the help of traction through this trocar, the appendix mesentery was dissected with a needle knife. Ligation of the appendix was done with absorbable loops. After dissection with an endoscopic scissor, the appendix was extracted via the oral route. Salpingo-oophorectomy was performed with the help of an intrauterine manipulator and a transvaginally introduced 5-mm trocar. After procedure, the posterior colpotomy was dilated and the specimens were extracted.

The gastric access was closed by an over-the-scope clip (OTSC 12/6a-220; Ovesco Endoscopy, Tübingen, Germany). Therefore, after fixation of the OTSC to the tip of the gastroscope, the latter was inserted carefully and a twin grasper was applied. This instrument enables the surgeon to grasp both edges of the gastric opening with subsequent independent locking (Fig. 1). After gastric full-thickness grasping of the gastric wall, the tissue was then pulled into the transparent hood of the gastroscope. The clip was released by a suture (Fig. 2). After extubation, all patients received double standard dose PPI (2 × 40 mg Panthocole, Nycomed S.C.A. SICAR, Opfikon, Suisse) for 8 days.

Results

Between April 2010 and March 2014, 43 patients underwent transgastric NOTES: 36 patients with an acute appendicitis, six patients with a prophylactic bilateral salpingo-oophorectomy because of the presence of BRCA1 or BRCA2 mutations, and one patient with uterus

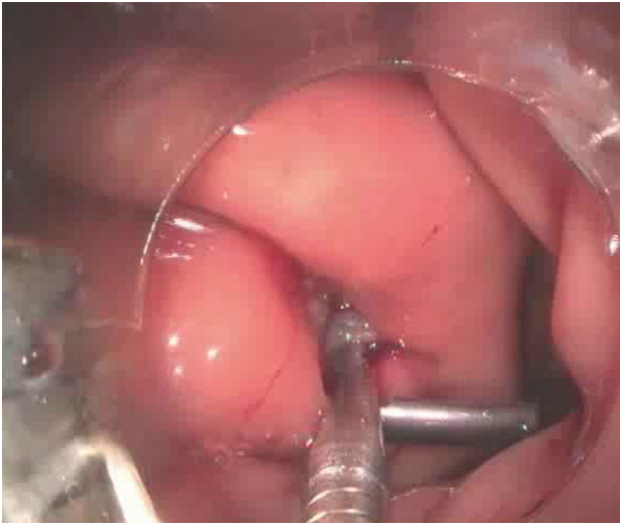


Fig. 1 Using a twin grasper to grasp both edges of the gastric opening independently

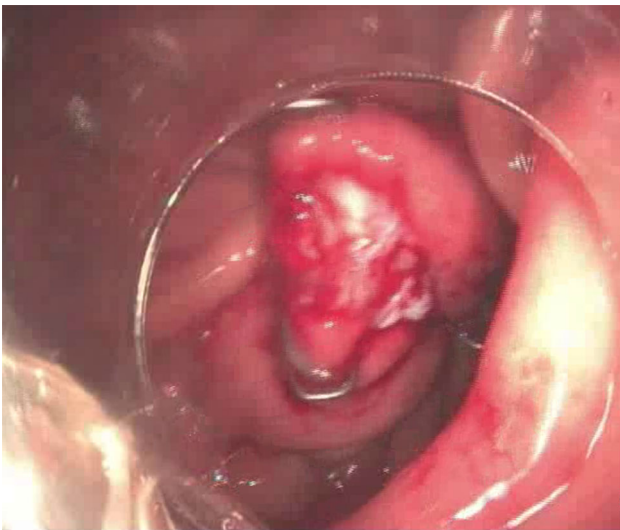


Fig. 2 Closed gastric opening after releasing the OTSC

myomatosis. The mean age was 34 years, and the mean body mass index (calculated as weight in kilograms divided by the square of height in meters) was 25.54. In all 43 cases, the incision of the gastric wall and the endoscopic access to the abdominal cavity succeeded without any difficulty. After performing the appendectomy in 36 cases, the bilateral salpingo-oophorectomy in six cases and the hysterectomy in one case, the gastric access was closed by releasing the OTSC. In all but one case, the OTSC was released without any problems and the visual tightness of the gastric closure was given. In one case after releasing the clip, there was still the defect of the gastric wall next to the OTSC. Thus, a second OTSC was added aside closing the defect completely.

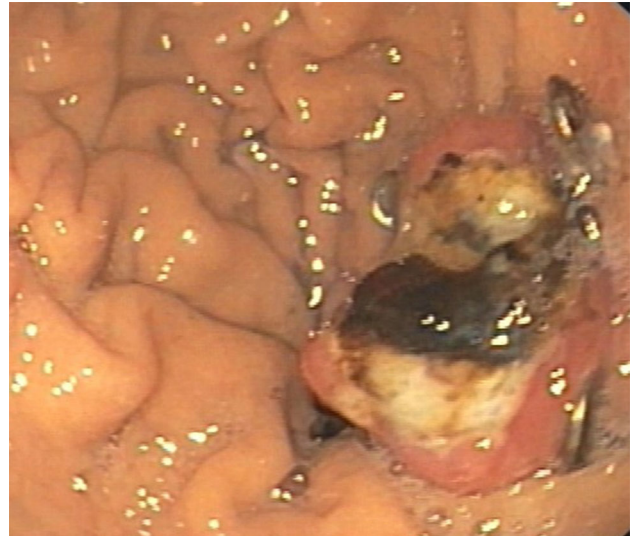


Fig. 3 Forrest IIb ulcer at the OTSC site

Regarding the closure of the gastric access, there were all in all three adverse events: one major (Clavien–Dindo Grade III) and two minor (Clavien–Dindo Grades I and II).

In two of the 43 cases (4.7 %), 2 days after the NOTES procedure, there was a decrease in the systemic hemoglobin with the clinical signs of an acute gastrointestinal bleeding; thus, an urgent gastroscopy was performed. In one of these cases, there were no signs of a former gastric bleeding during gastroscopy anymore. In the other case, there was a Forrest IIb ulcer at the OTSC site (Fig. 3); thus, four clips (Resolution™ Clip device, Boston Scientific Corporation, Natick, USA) were put prophylactic at the ulcer within the OTSC (Fig. 4). In both cases, there was no bleeding again and the patients could be discharged 2 days later without further problems. In one of the 43 cases (2.3 %), the patient developed signs of an acute upper peritonitis so a diagnostic laparoscopy was performed 2 days after the NOTES procedure. During laparoscopy, the finding was an insufficiency of the gastric closure with a local peritonitis; thus, the gastrotomy was closed with laparoscopic suturing and the abdominal cavity was cleaned with liquid solution. It was not the patient mentioned above needing two OTSC. With antibiotic therapy, no further problems occurred so the patient could be discharged 1 week later.

Discussion

NOTES is a technique in which an operation is performed within the body without a skin incision by using a natural body orifice to provide access. It has been described as the next surgical frontier with the objective of incision-free

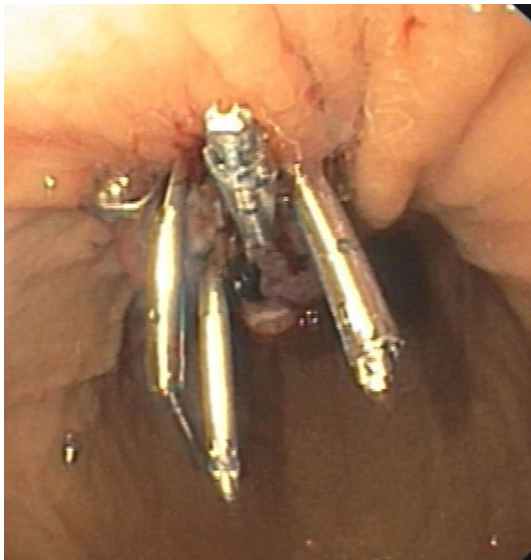


Fig. 4 Four endoscopic clips at the ulcer within the OTSC

abdominal surgery. Less surgical trauma and fast recovery are among the potential benefits of this minimally invasive surgical technique [10]. Transgastric access is preferred by some researchers due to its applicability to both sexes, a low risk for infection, and the great healing capability of the gastric wall. But closure of the gastric access may represent a crucial point in NOTES procedures. The general agreement is that there must be a minor tolerance for gastric leaks because there is no risk of gastric leaks using conventional or laparoscopic approaches [11]. That could be the reason why most human NOTES procedures have used a hybrid transvaginal access, limiting its use to females only [10]. Several devices have been tested in experimental settings for closure of transgastric access including endoscopic clips, Eagle Claws, threaded tags, staplers, and occluding systems [12]. Yet, the standard method and device for closure has not been defined. Potential devices that can achieve full-thickness gastrointestinal closure include the OTSC. The OTSC system has been studied extensively, and its use seems to provide an easy, safe, and reliable way to close gastrointestinal perforations and has even shown favorable results with regard to acute closure strength compared with surgical closures [8]. However, there are currently very limited data regarding the closure of transgastric NOTES procedures in humans. Herein, we first present a clinical series of 43 consecutive patients who underwent transgastric NOTES for different surgical procedures closing the access with the OTSC system. The focus of this study is the feasibility and safety of gastric closure. In all 43 cases, the incision of the gastric wall and the endoscopic access to the abdominal cavity succeeded without any difficulty for experienced endoscopists. Studies have shown that the OTSC is capable

of achieving full-thickness closure of gastrotomy defects [12]. The OTSC system has been studied extensively in experimental setting and has even shown favorable results with regard to acute closure strength compared with surgical closures. Delayed gastric emptying and chronic gastroparesis are well-known postoperative issues associated with gastric surgery. There is one animal study showing a negative impact on gastric motility due to the transgastric access [10]. In our clinical setting, these findings are not reproducible. After extubation, all patients received double standard dose PPI (2×40 mg Pantothole, Nycomed S.C.A. SICAR, Opfikon, Suisse) for 8 days. Oral intake of 500 ml cc tea was allowed on the first day, liquid food on the second day, and normal food on the third postoperative day. In these cases of closing the gastric access with an OTSC, transgastric access had no negative impact on gastric motility. No patient developed significant signs of gastrointestinal immotility.

Several studies have documented the histopathology of gastrotomies closed with OTSC [13]. Reported is full-thickness healing with mucosal ulcerations and mild foreign body reaction without ischemia or inflammation [14]. In two patients, we found similar results explaining the acute gastrointestinal bleeding 2 days after NOTES. In one case, we put four clips prophylactic at the ulcer within the OTSC. In both cases, it was a single bleeding without recurrence and the patients could be discharged 2 days later without further problems. Gastrointestinal bleeding after gastric closure with OTSC is possible, but it seems to be a minor complication sometimes requiring an endoscopic intervention. One of 43 patients developed a major complication. The patient developed signs of an acute peritonitis requiring a diagnostic laparoscopy 2 days after the NOTES procedure. But even in this case it was possible to handle the problem laparoscopically by closing the gastrotomy with laparoscopic suturing and cleaning the abdominal cavity adequate with liquid solution. With antibiotic therapy, no further problems occurred. We studied the OTSC system extensively in experimental setting and expanded training in animals. We know by experience that the OTSC usually closes the defect of the gastric wall after performing a balloon dilatation up to 20 mm and manipulating within the defect with a gastroscope completely. Accordingly, one OTSC should suffice to close the gastric access. Even it was not the patient mentioned above needing two OTSC, it is to be assumed that in this case the OTSC was placed insufficiently explaining the leakage in all probability.

The OTSC was released endoscopically, and the visual tightness of the gastric closure was given. Apparently, our adverse events were related to closure of gastrotomy. Although all these adverse events were successfully managed, the risk of transgastric NOTES is given as there is no

risk of conventional or laparoscopic approaches regarding the stomach. We should keep in mind that performing a save gastric closure with the OTSC is sophisticated and presumed a certain amount of experience in flexible endoscopy as well as in performing abdominal surgery in the case of treating a primary complication surgically. The main postulation to perform and to handle NOTES must be a well-trained physician in flexible endoscopy as well as in visceral surgery. It is important to keep in mind that these patients require careful assessment during the observation period following the procedure. If the patients develop signs of peritoneal contamination or abdominal sepsis, a surgical therapy must be taken into consideration. Even if we could show for the first time in more than 40 consecutive patients that there seems to be a safe approach for closing the transgastric access, it is absolutely necessary that further investigation in clinical settings has to be done to establish clear indications and guidelines for the use of transgastric NOTES.

Disclosures Ovesco Endoscopy (Tübingen, Germany) provided over-the-scope clips for the studies. Drs. Richard Magdeburg and Georg Kaehler have no conflict of interest or financial ties to disclose.

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