Transanal rectosigmoid resection via natural orifice translumenal endoscopic surgery (NOTES) with total mesorectal excision in a large human cadaver series

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Abstract

Background The authors' group has previously described successful transanal rectosigmoid resection via natural orifice translumenal endoscopic surgery (NOTES) in both porcine and cadaveric models using the transanal endoscopic microsurgery platform. This report describes the largest cadaveric series to date as optimization of this approach for clinical application continues.

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Methods Between December 2008 and September 2011, NOTES transanal rectosigmoid resection with total mesorectal excision (TME) was successfully performed in 32 fresh human cadavers using transanal dissection alone ($n = 19$), with transgastric endoscopic assistance ($n = 5$), or with laparoscopic assistance ($n = 8$). The variables recorded were gender, body mass index (BMI), operative time, length of the mobilized specimen, integrity of the mesorectum and the resected specimen, and complications. Univariate statistical analysis was performed.

Results Of the 32 cadavers, 22 were male with a mean BMI of 24 kg/m^2 (range 16.3–37 kg/m^2). The mean operative time was 5.1 h (range 3–8 h), and the mean specimen length was 53 cm (range 15–91.5 cm). After the first five cadavers, specimen length significantly improved, and a trend toward decreased operative time was demonstrated. The mesorectum was intact in 100 % of the specimens. In nine cadavers, endoscopic dissection was complicated by organ injury. Evaluation by the operative approach demonstrated a significantly longer specimen with laparoscopic assistance (67.7 cm) than with transgastric assistance (45.4 cm) or transanal dissection alone (49.2 cm) ($p = 0.013$). Comparison of the technique used for inferior mesenteric pedicle division demonstrated both significantly decreased operative time (4.8 vs 6 h; $p = 0.024$) and increased specimen length (57.7 vs 39.6 cm; $p = 0.025$) when a stapler was used in lieu of a bipolar cautery device.

Conclusion Transanal NOTES rectosigmoid resection with TME is feasible and demonstrates improvement in specimen length and operative time with experience. Transitioning to clinical application requires laparoscopic assistance to overcome limitations related to NOTES instrumentation, as well as procedural training with fresh human cadavers.

Natural orifice translumenal surgery (NOTES) likely represents the next step in the evolution of minimally invasive surgery. The proposed advantages of NOTES include faster recovery time, shorter hospital stays, improved pain control, and avoidance of potential abdominal wall complications including wound infection and hernia [1]. The range of operations currently under investigation is rapidly increasing. The international and national experience now counts several thousand cases of successfully performed hybrid transvaginal NOTES procedures including cholecystectomy, nephrectomy, and sleeve gastrectomy [2–8]. Progress, however, continues to be hampered by instrument and platform limitations as well as safety concerns regarding NOTES translumenal access.

Prior work has demonstrated transanal NOTES rectosigmoid resection to be safe and feasible in a swine model [7, 9]. The advantages of transanal access for colorectal resection are multiple. First, the availability of well-established platforms such as transanal endoscopic microsurgery (TEM) to gain access to the peritoneal cavity facilitates performance of endorectal and transrectal procedures [10]. Second, creation of the enterotomy though the organ to be resected rather than an otherwise healthy organ obviates concerns regarding safe, reproducible closure associated with other NOTES access points.

In 2007, Whiteford et al. [11] described the first transanal NOTES radical sigmoidectomy in human cadavers. Although colon and mesenteric dissection could be technically achieved using the TEM platform, difficulties were encountered with mobilization of adequate specimen length resulting from instrument inability to overcome anatomic constraints [4].

Although instrument and platform limitations continue to be a barrier to pure application of transanal NOTES resection, ongoing work has resulted in worldwide human clinical case reports, [8, 12, 13]. As transition to human application continues, optimization of this technique and procedural training are imperative.

The following study represents our experience with transanal NOTES rectosigmoid resection in the largest reported cadaveric series to date. This study aimed to outline the procedural steps and the learning curve associated with tranasanal NOTES rectosigmoid resection. In addition, we aimed to highlight the importance of cadavers as an essential training model for the safe adoption of this procedure.

Materials and methods

Between December 2008 and September 2011, transanal NOTES rectosigmoid resection was performed successfully in 32 fresh human cadavers. The rectosigmoid resections were performed either by transanal dissection alone ($n = 19$), with transgastric endoscopic assistance ($n = 5$), or with laparoscopic assistance ($n = 8$). The primary objective of this study was to optimize the technique of NOTES transanal rectosigmoid resection with total mesorectal excision (TME) before human clinical application. The secondary objective was to achieve the maximum length of sigmoid mobilization using a NOTES approach. The variables recorded were gender, body mass index (BMI), operative time, operative approach, maximum length of the mobilized specimen, integrity of the mesorectum and resected specimen, and operative complications.

Operative technique

Transanal dissection

The rectum was occluded transanally with a 2-0 Vicryl purse-string suture approximately 3–4 cm from the anal verge, above the sphincter complex. The 7.5-cm TEO proctoscope (Storz, Tuttlingen, Germany) then was inserted transanally and sealed with a faceplate. Next, low-pressure CO_2 (9 mmHg) was insufflated (Fig. 1A).

Circumferential dissection of the rectum was initiated above the anal sphincter complex using electrocautery and TEO dissecting instruments. Posterior entry into the presacral space was facilitated by CO_2 insufflation and flexible-tip instruments. The mesorectum was mobilized sharply, with or without electrocautery or a bipolar device (Autosonix ultrashears, Covidien, Norwalk, CT), and mesorectal dissection proceeded cephalad along the avascular presacral plane (Fig. 1B). This plane of dissection was extended medially, laterally, and anteriorly to achieve circumferential rectal mobilization and TME. The shorter proctoscope was replaced with the 15-cm proctoscope to improve exposure.

The peritoneal reflection was visualized and divided anteriorly after careful mobilization of the vagina or prostate from the anterior rectal wall, and the peritoneal cavity was entered. The peritoneal attachments of the rectosigmoid were divided using electrocautery and a bipolar device (Autosonix). Proximal dissection was continued either via transanal endoscopic dissection alone or with transgastric endoscopic or laparoscopic assistance (Fig. 1C). The inferior mesenteric pedicle was divided in all cadavers using a bipolar device or a linear endoscopic
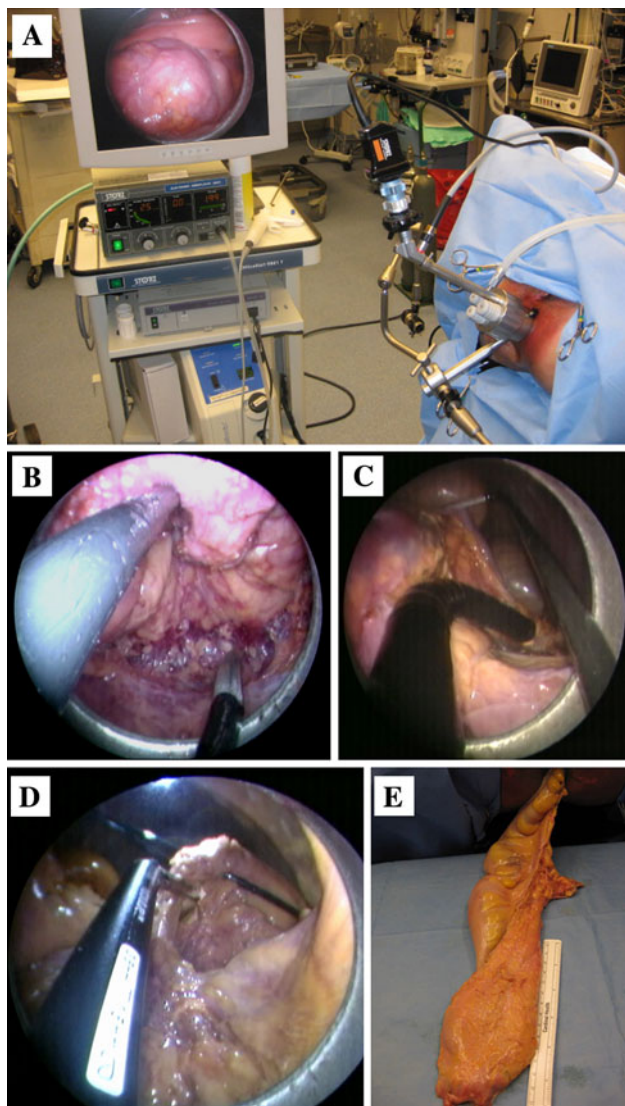
Fig. 1 Transanal rectosigmoid resection via natural orifice translumenal endoscopic surgery (NOTES) in a female cadaver. **A** The TEO platform is used to initiate full-thickness rectal and mesorectal endoscopic dissection. **B** Total mesorectal dissection is completed posteriorly. **C** After transanal peritoneal entry, the sigmoid is mobilized using laparoscopic instruments and a gastroscope inserted transanally. **D** Laparoscopic assistance during transanal transection of the inferior mesenteric pedicle (IMA) with a stapler. **E** Transanal extraction of the specimen demonstrating integrity of the mesorectum

stapler (EndoGIA; Covidien) inserted transanally through the TEO platform (Fig. 1D).

Pure transanal endoscopic dissection (n = 19)

After transanal entry into the peritoneal cavity, dissection was extended as cephalad as possible using TEO and laparoscopic instruments, with or without transanal endoscopic assistance using a gastroscope (Pentax Medocal

Inc., Montvale, NJ, USA). When dissection could not be extended any further, the proctoscope was removed, and the specimen was exteriorized in preparation for specimen extraction.

Of the 19 cadaveric operations performed via a pure transanal approach, two were carried out using laparoscopic and TEO instruments through the TEO platform, eight using endoscopic assistance with a gastroscope (Pentax) inserted through the TEO platform, and nine using endoscopic assistance through a novel rigid endoscopic platform inserted through the TEO platform (ISSA; Storz). The purpose of this novel platform was to provide additional rigidity to the gastroscope.

Transgastric endoscopic assistance (n = 5)

Transgastric assistance was performed as previously described [8]. In brief, after maximal transanal rectosigmoid mobilization, peroral transgastric peritoneal access was obtained using a 12.8-mm colonoscope (Pentax). A 4-mm gastrotomy then was made using a needleknife (Cook Medical Inc., Winston-Salem, NC, USA) and dilated.

Once access was established, the colonoscope was advanced into the peritoneal cavity. In two cases, transgastric access and dissection were performed using a novel endoscopic platform (Anubiscope; Storz). The lateral peritoneal attachments of the rectosigmoid, sigmoid, and descending colon then were divided using the needleknife. Transanal and transgastric mobilization were combined until no further mobilization could be safely achieved.

Laparoscopic assistance (n = 8)

For operations performed with laparoscopic assistance, one to three abdominal trocars were inserted to improve visualization or to facilitate colon retraction. This permitted more proximal dissection of the rectosigmoid junction achieved transanally through the TEO platform.

Transanal rectosigmoid resection and anastomosis

Once the rectosigmoid specimen had been fully mobilized, it was exteriorized, measured, and subsequently transected (Fig. 1E). A Lone Star retractor (Cooper Surgical, Trumbull, CT, USA) then was positioned and a handsewn coloanal anastomosis performed between the proximal sigmoid colon and the distal anorectal cuff, as previously described [8].

Statistical analysis

Univariate analysis by unpaired t-test with two-tailed distribution was used for quantitative variables, and χ^2 was

used for categorical variables. All p values lower than 0.05 for associations were considered to indicate statistical significance. Prism statistical software (April 2003) (Prism Software Corporation, Irvine, CA, USA) was used for all analyses.

Results

Of the 32 fresh human cadavers, 22 were male and ten were female. The mean body mass index (BMI) was 24 kg/m^2 (range 16.3–37 kg/m^2). Overall, the mean operative time was 5.1 h (range 3–8 h), and the mean length of the mobilized specimen was 53.2 cm (range 15–91.5 cm). An EndoGIA stapler was used to divide the inferior mesenteric pedicle in 23 cadavers versus a bipolar cautery device used in nine cadavers. Rectosigmoid resection was successfully completed in all 32 cadavers, and the mesorectum was intact in all the specimens. Nine operative complications occurred.

Operative approach

Comparison by operative approach demonstrated a significantly longer specimen with laparoscopic assistance (67.7 cm) than with transgastric endoscopic assistance (45.4 cm) or transanal dissection alone (49.2 cm) ($p = 0.013$). Transgastric endoscopic assistance did not increase the mean specimen length of the colon retrieved compared with transanal mobilization alone. With respect to a pure transanal endoscopic approach, when comparing transanal dissection with TEO, TEO with endoscopic assistance using a transanal gastroscope, and TEO with endoscopic assistance using the ISSA platform, no significant difference in specimen length or operative time, complications, or BMI was demonstrated between the approaches (Table 1).

Inferior mesenteric pedicle division

Assessment of the method used for inferior mesenteric pedicle division demonstrated a statistically significant decrease in operative time (4.8 vs 6 h; $p = 0.024$) and an increased specimen length (57.6 vs 39.6 cm; $p = 0.025$) when an EndoGIA stapler was used versus a bipolar device, respectively. Although not statistically significant, a trend toward fewer intraoperative complications in the stapler group (21 %) than in the bipolar device group (44 %) ($p = 0.086$) also was noted. No other difference was demonstrated by BMI, cadaveric quality, gender, or operative approach.

Table 1 Comparison by operative approach

	TA (n = 19)	TA + TG (n = 5)	TA + LAP (n = 8)	p Value
Gender: n (%)				
Male	11 (58)	4 (80)	7 (87.5)	NS
Female	8 (42)	1 (20)	1 (12.5)	
BMI (kg/m^2)	24	24.7	23.6	NS
Specimen length (cm)	49.2	45.4	67.7	0.013
Range	(15–75)	(15–67)	(47–91.5)	
Operative time (min)	302	310	288.8	NS
Range	(210–410)	(180–480)	(180–390)	
Complications: n (%)	5 (26)	3 (60)	1 (12.5)	NS
Colon/rectal perforation	5	3	0	
Small bowel enterotomy	0	1	0	
Vaginal perforation	0	0	1	

TA transanal, *TG* transgastrically assisted, *LAP* laparoscopically assisted, *NS* not significant, *BMI* body mass index

Complications

Nine operative complications occurred as follows: colon perforation ($n = 5$), rectal perforation ($n = 2$), vaginal perforation ($n = 1$), and small bowel enterotomy ($n = 1$). No difference in complication rate was demonstrated by BMI, gender, operative time, or length of the specimen retrieved. However, factors associated with complications included poor quality of the cadaver ($n = 3$), a prior pelvic operation ($n = 3$), and a very redundant sigmoid ($n = 1$). Although not statistically significant, a trend toward decreased complications was demonstrated by operative approach, with the combined transanal and laparoscopic approach resulting in the lowest rate of complications compared with the transanal approach alone or with transgastric assistance (12.5 vs 26 vs 60 %), respectively (Table 2).

Learning curve

A significant increase in specimen length was demonstrated after the first five cadavers regardless of the operative approach (28.2 vs 57.9 cm; $p = 0.001$) as well as a decrease in operative time (5.9 vs 4.9 h; $p = 0.13$). No other difference was demonstrated by cadaveric gender, mean BMI, cadaveric quality, or complication (Fig. 2A, B).

Table 2 Rate of operative complications

	Complication (n = 9)	No complication (n = 23)	p Value
Gender: n (%)			
Male	5 (55)	17 (74)	NS
Female	4 (45)	6 (26)	
BMI (kg/m^2)	23.3	24.3	NS
Specimen length (cm)	50.0	54.3	NS
Range	(15–72)	(15–91.5)	
Operative time (h)	5.1	5.1	NS
Range	(3–8)	(3–7)	
Operative approach			NS
Transanal (n = 19)	5	14	
Transanal + transgastric (n = 5)	3	2	
Transanal + laparoscopic (n = 8)	1	7	
Inferior mesenteric pedicle division			NS
Stapling device (n = 23)	5	18	
Electrocautery (n = 9)	4	5	

NS not significant, BMI body mass index

Discussion

Transanal NOTES rectosigmoid resection with TME is a feasible and promising approach for patients with rectal cancer. Appropriate training is essential for safe adoption of this procedure because inadequate oncologic resection and major complications are technical errors with severe adverse consequences. Evaluation of our series of 32 cadavers demonstrated several crucial points pertaining to this procedure. Specifically, key information was garnered regarding operative approach, specimen length, complication rate, and adequacy of oncologic resection.

It is not surprising that the addition of laparoscopic assistance significantly increased the length of the specimen retrieved. As we observed in our prior swine studies, transanal endoscopic mobilization of the proximal colon and mesocolon is severely limited due to difficulties with retraction and exposure by conventional laparoscopic and endoscopic instruments [7, 9]. This finding reiterates the necessity for the development of improved platforms and instruments to overcome technical limitations once the peritoneal cavity is entered. The unexpected finding, however, was that the addition of transgastric assistance did not improve the length of the specimen retrieved compared with transanal resection alone. This observation is disparate from our previous findings in a swine model [7].
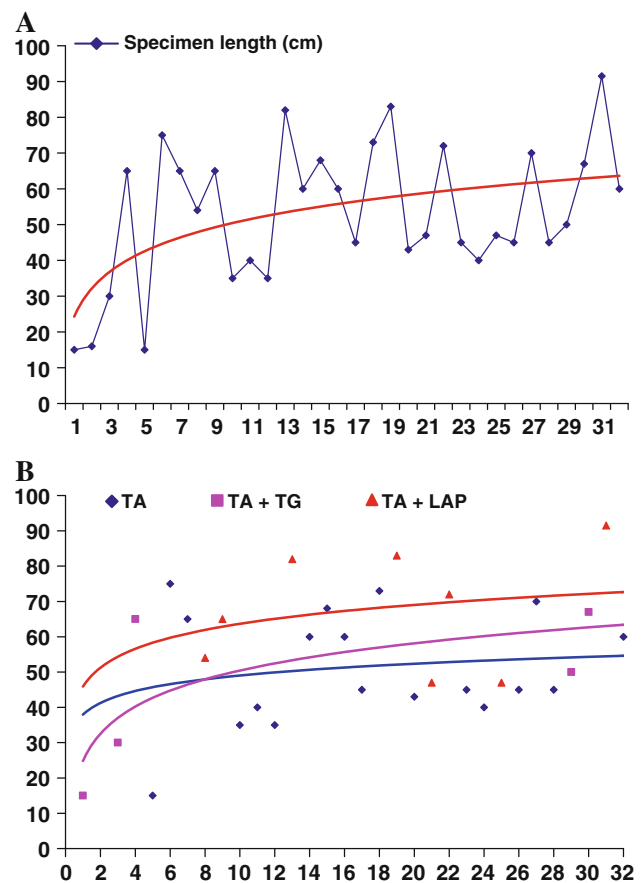

Fig. 2 A Specimen length by individual cadaver. **B** Specimen length by operative approach and individual cadaver

Several factors may account for this finding. First, increased experience with transanal dissection alone has significantly improved the length of colon that can be mobilized proximally. This theory is substantiated by our data, which demonstrate a significant correlation between improved specimen lengths and the number of cadavers that underwent the procedure. Second, technical limitations are associated with transgastric NOTES access. As with transanal resection, instrument limitations continue to hinder transgastric NOTES procedures. The lack of sturdy, flexible-tip instruments make dissection and colonic manipulation challenging. Finally, transgastric assistance was attempted with only five cadavers (15 %), so the results may be biased given the small sample size.

Based on these findings, at this writing, we recommend that transgastric assistance should remain an experimental adjunct to transanal NOTES rectosigmoid resection. Further investigation in the laboratory, improved instrumentation, and proven reliable gastric access closure are needed before pure application of transanal/transgastric NOTES rectosigmoid resection in humans.

Another interesting finding pertained to division of the inferior mesenteric pedicle as it related to specimen length and operative time. This study demonstrated that division of the inferior mesenteric pedicle with an EndoGIA stapler rather than a bipolar device resulted in significantly increased specimen length and decreased operative time. Although not significant, a trend toward a decreased incidence of intraoperative organ injury also was observed. One likely explanation for this finding pertains to patient anatomy. The decision to divide the inferior mesenteric pedicle by a stapling device instead of electrocautery was largely based on mesenteric configuration. Stapling devices were used with more favorable anatomic configurations where the mesentery was well aligned. Anatomy favoring a less technically challenging dissection potentially explains increased specimen length, decreased operative time, and the observed decreased rate of complication.

With respect to the adequacy of transanal endoscopic rectosigmoid and mesorectal resection, adequate oncologic resection was accomplished successfully in all cadavers, as illustrated by the fact that the mesorectum was intact in all the specimens. The rate of intraoperative complications in this series was 28 %. Although no statistically significant parameter could be correlated with increased risk of complication, several associated factors were identified. Poor cadaver quality and prior pelvic operation were the two variables most frequently associated with organ injury during endoscopic dissection. Although not statistically significant, the lowest complication rate occurred for cadavers undergoing laparoscopically assisted transanal NOTES rectosigmoid resection. Only one complication, vaginal perforation, occurred in this group and involved a cadaver that had undergone previous transabdominal hysterectomy with difficult dissection due to the presence of a rectocele.

The rate of complications associated with pure NOTES rectosigmoid resection again highlights the importance of continued technique development and optimization in the laboratory setting. This finding also reiterates the necessity of careful patient selection for human trials as well as the necessity, currently, for laparoscopic assistance during NOTES transanal TME.

The limitations of the current study included the descriptive nature of the study as well as the disparate sample size in comparative arms, which may have biased results. Nonetheless, this study represents the largest series of cadavers undergoing transanal NOTES rectosigmoid resection and provides valuable information regarding the feasibility and safety of this procedure. In particular, this study highlights the steep learning curve associated with this approach and the fact that a complete TME can be achieved in every male and female cadaver using a transanal endoscopic approach.

As previously shown in both a survival swine model and other cadaver investigations, this study also demonstrated the technical challenges of proximal colon mobilization using a pure NOTES approach, as highlighted by the 28 % incidence of organ injury during transanal endoscopic dissection [7, 14]. Based on this extensive experience, we conclude that procedural training with human cadavers is essential for the transition to clinical application of transanal endoscopic NOTES rectosigmoid resection. In addition, laparosocopic assistance is required to overcome the limitations in NOTES instrumentation and to ensure safety.

Conclusion

Transanal NOTES rectosigmoid resection with TME is feasible in a cadaveric model, with demonstrated improvement in specimen length and operative time with experience. Continued development of new endoscopic and flexible-tip instruments is imperative before clinical application of pure NOTES. We strongly advocate procedural training in fresh human cadavers before human application.

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