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Intra-abdominal bacterial contamination in TAMIS total mesorectal excision for rectal carcinoma: a prospective study

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Abstract
Background Natural orifice transluminal endoscopic surgery (NOTES) is currently gaining a lot of attention. NOTES is expected to further reduce surgical trauma and improve patient care due to eliminating abdominal incisions. The interest in transrectal NOTES has grown slowly, because of concerns of bacterial contamination due to transection of the rectum at the start of the procedure. However, different studies already demonstrated that transanal TME (TaTME) can be performed without major complications. This prospective study focuses on the presence and clinical significance of peritoneal bacterial contamination after TaTME for rectal cancer.
Methods Three bacterial cultures were taken at standardized locations from the pelvic area after completion of the TaTME procedure and before closure of the incisional wounds. The cultures were evaluated for bacterial count and species identification. Furthermore, C-reactive protein and white blood cell count were measured perioperatively, and postoperative complications were recorded.
Results Twenty-three consecutive patients were included between July 2013 and December 2014. Thirty-nine percent (9/23) of the cultures showed gastrointestinal flora. Four of these patients (44 %) developed presacral abscesses. The remaining 61 % (14/23) of the cultures were negative. None of these patients developed infectious complications.
Conclusion Transanal TME procedures are associated with positive cultures in more than one-third of the patients. In these patients, postoperative locoregional infectious complications are more common.

Keywords TaTME · TAMIS · NOTES · Rectal cancer · Rectal carcinoma · Infection

In the last 20 years, endoscopic minimally invasive techniques have replaced the open approach for many surgical procedures. Patients benefit from the reduction in surgical trauma with a proven decrease in morbidity, a shorter hospital stay and a faster recovery.

In 2004, natural orifice transluminal endoscopic surgery (NOTES) was presented as the next 'holy grail' in surgery. NOTES makes abdominal incisions unnecessary and is therefore expected to further improve patient care [1]. The majority of published articles have focused on the transgastric technique, because the stomach was expected to be the most accessible NOTES entrance to the peritoneal cavity at the lowest risk. In contrast to the transgastric approach, the transrectal NOTES was considered less safe due to the high risk of bacterial contamination from the rectum loaded with microorganisms.

Currently, the opinion on NOTES has changed significantly; technical limitations have slowed down most research on transgastric NOTES. Interestingly, transrectal NOTES is now gaining more attention. Various authors described the feasibility of transanal dissection of the mesorectum in patients with rectal cancer. In theory, this

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technique has great advantages over open and traditional laparoscopic total mesorectal excision (TME) because of better visualization of the distal part of the rectum which can improve the quality of surgery [2].

However, concerns exist about the safety of transanal TME (TaTME), because of the iatrogenic perforation of the rectum and the possible bacterial contamination potentially resulting in intra-abdominal infections.

This article describes the results from a prospective study on the presence and clinical significance of peritoneal bacterial contamination during TaTME for rectal cancer.

Methods

After institutional review board approval, a prospective cohort study of patients undergoing a TaTME for rectal cancer was performed at Gelderse Vallei Hospital between July 2013 and December 2014. Patients with an indication for an abdominoperineal resection (APR) were excluded. The study was conducted in collaboration with the institutional Department of Microbiology.

For inclusion, patients had to be diagnosed with rectal carcinoma by colonoscopy or proctoscopy, histologically proven through biopsy. All patients were treated according to the Dutch guidelines for the treatment of rectal cancer.

Preoperative preparation

According to the institutional routine practice, all patients received oral bowel preparation with Moviprep (Norgine, Amsterdam, the Netherlands) the day before surgery. A single dose of 2 g of cefazolin and 500 mg of metronidazole were administered during anesthetic induction and repeated when surgery took more than 3 h. No prophylactic antibiotics were given postoperatively.

Surgical procedure

TaTME was performed as described earlier by Velthuis et al. [2] with the following modifications. The procedure is now standardized and starts with the transabdominal phase instead of the transanal phase. In the abdominal phase, the sigmoid and splenic flexure are mobilized from medial to lateral by multiport laparoscopy or through single-port surgery with the single port located in the future ileostomy side [3]. The inferior mesenteric artery is ligated using the Ligasure device (Covidien, Mansfield, MA, USA) after identification of the left ureter. After mobilization of the descending colon, sigmoid and the proximal rectum, the transanal phase is initiated. Following closure of the rectal stump, the cavity is rinsed with a povidone-iodine solution (Betadine, Purdue, Stanford, CA USA). The TaTME is further continued as described by Velthuis et al. All TaTMEs were performed by one experienced laparoscopic surgeon (CS).

In short, with the use of a transanal port (Applied Medical, Rancho Santa Margarita, CA, USA), the rectum is insufflated and thereafter closed with a purse string suture. The lumen is rinsed again with a povidone-iodine solution. The TME mucosa is dissected with the use of a diathermic hook, and thereafter, the TME plane is dissected, beginning dorsally continuing as high up as possible. Then, the ventral plane is dissected and at the end, both planes are connected. After full mobilization, the specimen is extracted transanally and a stapled anastomosis is made with the use of an EEA hemorrhoid stapler (Covidien, Mansfield, MA, USA).

Microbiologic samples and analysis

After completion of the TaTME procedure and after specimen extraction, three bacterial cultures were taken from the pelvic area in every patient. The cultures were taken at standardized locations, ventrally from the prostatic or posterior vaginal wall, from the posterior pelvic floor and intra-abdominally near the promontory. The cultures were obtained with swabs through the laparoscopic ports and collected in sterile containers. The cultures were evaluated at the institutional Department of Microbiology for bacterial count and species identification. Both direct bacteriological examination and routine aerobe and anaerobe bacterial cultures were performed on the samples.

Clinical data

Postoperative complications were recorded prospectively during hospital or during 3 weeks. C-reactive protein (CRP) and white blood cell count (WBC) were measured on day 1, day 3 and day 5 postoperatively and recorded.

Results

Twenty-three consecutive patients who underwent a transanal TME because of a rectal carcinoma were included. Baseline and endpoint results are depicted in Table 1. No intraoperative complications occurred. Mean operation time was 204 min with a variation from 152 to 248 min.

Culture results and clinical relevance

Sixty-one percent (14/23) of the patients had negative abdominal cultures. None of these patients developed infectious complications.

Table 1 Patient characteristics and study results

Patient	Neoadjuvant therapy	pTNM	Cultures	Infectious complications	Therapy
1	5 × 5 Gy	T2N0	n.g.	No	n.a.
2	5 × 5 Gy	T3N0	Sporadic mixed aerobic + anaerobic flora	Small presacral abscess	Manual drainage
3	CH-RT	T3N0	Sporadic *E. coli*	No	n.a.
4	5 × 5 Gy	T2N0	n.g.	No	n.a.
5	5 × 5 Gy	T2N0	n.g.	No	n.a.
6	5 × 5 Gy	T2N0	Sporadic *E. coli*	Presacral abscess	Manual drainage
7	5 × 5 Gy	T2N0	Sporadic *E. coli*	No	n.a.
8	5 × 5 Gy	T2N0	Sporadic *E. coli* + *S. bovis* II + *E. casseliflavus*	No	n.a.
9	5 × 5 Gy	T2N0	Sporadic *E. col*i	Presacral abscess	Manual drainage
10	CH-RT	T3N1	n.g.	No	n.a.
11	5 × 5 Gy	T2N0	Sporadic *E. coli*	No	n.a.
12	No	T3N0	n.g.	No	n.a.
13	No	T2N1	n.g.	No	n.a.
14	CH-RT	T3N0	Sporadic pseudomonas aeruginosa, multiple anaerobic flora	Presacral abscess	Antibiotics
15	CH-RT	T2N0	n.g.	No	n.a.
16	5 × 5 Gy	T3N1	n.g.	No	n.a.
17	No	T2N1	n.g.	No	n.a.
18	5 × 5 Gy	T2N0	n.g.	No	n.a.
19	5 × 5 Gy	T2N0	Sporadic *E. coli*	No	n.a.
20	No	T3N0	n.g.	No	n.a.
21	5 × 5 Gy	T2N1	n.g.	No	n.a.
22	5 × 5 Gy	T2N2	n.g.	No	n.a.
23	No	T2N0	n.g.	No	n.a.

Escherichia coli (*E. coli*), *Streptococcus bovis* II (*S. bovis* II), *Enterococcus casseliflavus* (*E. casseliflavus*)

TNM tumor node metastasis criteria 5th edition, *pTNM* pathological tumor node metastasis, *n.g.* no growth, *n.a.* not applicable, *Gy* gray, *CH-RT* chemoradiotherapy

Nine patients (39 %) had positive bacterial cultures. The exact species are depicted in Table 1. The majority of these cultures showed sporadic growth of *Escherichia coli* (*E. coli*). One culture showed Pseudomonas aeruginosa. Four of these patients (44 %) actually developed a presacral abscess, of which one patient had an anastomotic leakage which required reoperation. In this patient, an ileostomy was already created in the primary operation so leaving drains during reoperation was sufficiently. In a later stadium, a successful restoration of intestinal continuity was performed without the development of new anastomotic leakage or abscess. Two of the other three patients were treated with manual rectal drainage, without the need for re-intervention. The fourth patient was successfully treated with antibiotics. In the remaining five patients, the sporadic presence of *E. coli* did not lead to any infectious complications.

There was no correlation between operation time and culture results or infectious complications in this study.

C-reactive protein, white blood cell count and clinical relevance

Mean CRP levels in patients with negative cultures were 86 mg/l on day 1, 121 mg/l on day 3 and 76 mg/l on day 5 postoperatively. In case of positive cultures, mean CRP levels were higher: 126 mg/l on day 1, 147 mg/l on day 3 and 135 mg/l on day 5. Mean WBCs were similar between patients with negative and positive cultures: 9/nL on day 1, 9/nL on day 3 and 8.5/nL on day 5.

Discussion

In this study, we have demonstrated the occurrence of abdominal bacterial contamination during TaTME procedures. Patients with positive cultures had an increased risk on the development of infectious complications. None of the patients developed clinically severe infections.

Thirty-nine percent (9/23) of the cultures showed gastrointestinal flora and four of these patients actually developed a presacral abscess. None of the patient with negative cultures developed infectious complications.

A relatively high percentage (17 %) of infectious complications was observed in the total group of TaTME patients. Our overall results, however, do not suggest an increase in morbidity when compared with the regular laparoscopic TME. We recently reported an overall morbidity of 39 % in a cohort of 80 patients who underwent a TaTME. This is comparable with the short-term results from the COLOR II trial [4].

Since the introduction of NOTES by Kalloo et al. [5], a lot of experimental and clinical studies have been published on bacterial translocation during these procedures. Most research focused on transgastric and transvaginal procedures. Transgastric NOTES was expected to be the preferred excess route with a low risk of bacterial contamination and moreover suitable in both men and women. Research showed that the transcolonic approach carries the highest risk of bacterial contamination, followed by transgastric, transesophageal, transvaginal and transvesical techniques [6].

In 2011, Memark et al. [7] published their study results on infectious complications after 40 transgastric endoscopic peritoneoscopies. All the patients received prophylactic intravenous penicillin or 2 g of cefazolin at induction. The procedures were performed without preoperative gastric decontamination. The authors concluded that contamination of the peritoneal cavity does occur, however, does not lead to a significantly increased risk of infectious complications. They also state that gastric decontamination is not necessary in case of transgastric endoscopic peritoneoscopy.

Linke et al. [8] measured the extent of microbiological contamination of the peritoneal cavity after a transvaginal NOTES access and the effect of preoperative vaginal disinfection on vaginal colonization. They demonstrated microbiological contamination of the peritoneal cavity in a minority of patients during a hybrid transvaginal cholecystectomy after vaginal disinfection with hexetidine tablets and octenidine. No postoperative surgical site infections occurred. Other clinical studies on hybrid transvaginal cholecystectomies, including one of our own study groups [9], have also documented very few cases of postoperative infections [10–12].

In contrast to the previously described transgastric and transvaginal NOTES techniques, transrectal NOTES was initially considered not applicable due to the high bacterial load in the rectum and the feared associated infectious complications. However, through the years, transrectal NOTES has gained interest after the success stories about transanal endoscopic microsurgery (TEM). Since then, several experimental transrectal NOTES studies of different kinds have been published.

Initially, researchers performed transrectal access and closure studies on animal models. Diana et al. [13] performed an experimental study of transrectal viscerotomy closure in porcine models. As a secondary outcome, they measured bacterial contamination and found that all of 12 pigs had enteric bacterial contamination of the peritoneal fluid after viscerotomy. However, only one pig developed a postoperative wound infection.

Clinical human data show comparable results. Leroy et al. [14] performed a prospective study on 16 consecutive patients who underwent a laparoscopic sigmoid colectomy with transanal specimen extraction for previous diverticulitis. Although they found polybacterial growth in all peritoneal culture samples after systematic intra-operative bacteriological sampling, no infection-related complications were observed.

Currently, most surgeons who perform TaTMEs use a povidone-iodine solution to rinse the rectum before and during the procedure. Whether this has any effect on bacterial contamination or the occurrence of infectious complications is not clear.

Within the urology department, several randomized controlled trials have been performed on rectal cleansing with povidone-iodine before performing a transrectal ultrasound-guided prostate biopsy. The results were variable. Abughosh et al. [15] did not find any significant evidence for rectal cleansing in a total study group of 865 men. However, Ghafoori et al. [16] did find a significant difference between their cleansing group and their control group in favor of the cleansing group regarding the occurrence of infectious complications. This study also comprised a randomized controlled trial with a total of 280 patients.

Goh et al. [17] stated that the rectum is probably not the most ideal environment for optimal bactericidal effect of povidone-iodine. According to the authors, this can be explained by two reasons. First, free iodine is adsorbed on the surface of organic material, including fecal material, mucus and debris from mucosal lining. Therefore, the efficacy of free iodine will be reduced in the rectum [18]. Furthermore, drying of the iodophor is necessary to optimize the effect of the povidone-iodine solution [19]. With the rectum being an enclosed cavity, drying of the iodophor is limited. There are indications that chlorhexidine gluconate is a better alternative to povidone-iodine [17]. However, no randomized controlled research is still performed on the effect of chlorhexidine gluconate in neither transrectal prostatic biopsy nor surgery.

In conclusion, the current data suggest that TaTME is associated with a risk of bacterial contamination. In patients with positive cultures, postoperative locoregional

infectious complications are more common compared with patients with negative cultures. The effect of the type of disinfectant or duration of perioperative antibiotics needs to be studied further.

Disclosures S. Velthuis, M. Veltcamp Helbach, J. B. Tuynman, T. Le, H. J. Bonjer, and C. Sietses have no conflicts of interest or financial ties to disclose.

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