Short-Term Outcomes and Oncologic Clearance of Side-to-End Anastomosis after Low Anterior Resection in Rectal Cancer Patients

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Background: *Low anterior resection (LAR) is the procedure of choice to achieve oncologic resection and sphincter saving for rectal cancer patients. Although outcomes of side-to-end anastomosis after LAR were acceptable, most studies reported only a small number of cases and studies in Thai patients are limited.*
Objective: *To determine short-term outcomes and oncologic clearance of side-to-end anastomosis after low anterior resection in rectal cancer patients.*
Material and Method: *A retrospective patient charts review was performed. All patients with pathologically confirmed adenocarcinoma of the rectum who underwent LAR with side-to-end anastomosis in the Colorectal Surgery Unit, Department of Surgery, Faculty of Medicine Siriraj Hospital between July 2007 and April 2010 were included. Demographic, perioperative data and postoperative short-term outcomes were analyzed.*
Results: *There were 113 patients with a mean age of 60 years; 57 (50.4%) males and 56 (49.6%) females. Six percent of the patients underwent preoperative neoadjuvant chemo-radiation. The average tumor location was 6.7 cm above the anal verge; 31 (27.4%) above, 37 (32.7%) at and 45 (39.8%) below the peritoneal reflection. Pathologically, most specimens were T3 tumors (67.3%) and half of the patients had positive lymph nodes. The median number of harvested lymph nodes was 18 and the resected surgical margins were 6.1% microscopically positive. The overall postoperative complication rate was 38.9%, anastomosis leakage rate was 6.2% and there was one death. The median time to regular diet resumption was 110 hours and the median hospital stay was 11 days.*
Conclusion: *Short-term outcomes and oncologic clearance of low anterior resection with side-to-end anastomosis is comparable to reported outcomes in other studies. Long-term oncologic and functional outcomes need to be studied further.*

Keywords: *Rectal cancer, Low anterior resection, Side-to-end anastomosis, Short-term outcomes, Oncologic clearance*

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Colorectal cancer is one of most common cancer in Thai population[1]. Majority of colorectal cancer occur in the left-side colon especially rectum[2,3]. The first two principles of rectal cancer surgery consist of either achieving oncologic outcomes which could be demonstrated by pathological specimen clearance and sphincter saving. Low anterior resection (LAR) is the procedure of choice to serve for these two purposes especially when tumors locate astride or below peritoneal reflection.

Functional outcomes and quality of life are other concerns in patients who underwent low anterior resection for rectal cancer[4]. Patient who underwent LAR and simply reconstructed anastomosis with straight end-to-end colorectal anastomosis could have problems with frequent bowel movements, fecal urgency and incontinence[5]. These sequelae were well known as an anterior resection syndrome which usually temporarily occurs and improves in the first year after surgery[6]. Several methods of colorectal anastomosis such as colonic J-pouch, transverse coloplasty and side-to-end anastomosis (Baker) have been developed as alternative surgical techniques in order to resolve this problem[7]. Colonic J-pouch could be created by either hand-sewn or staple. The principle of creating

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this pouch is to build a new reservoir or neo-rectum. However, this method is not suitable in some patients whose pelvic cavity were narrow because creation of anastomosis is difficult. Transverse coloplasty (TCP) seems to answer this drawback of colonic J-pouch. Although technique of performing TCP is more simple because of no need to perform a pouch and functional outcomes after these two procedures are comparable, some studies reported a slightly high leakage rate of TCP[7]. Meanwhile, side-to-end anastomosis seems to include advantages of both colonic J-pouch and TCP[8,9]. To date, recent systematic review and studies compared results among these anastomosis techniques and reported no significant difference in functional outcomes as well as postoperative short term results[10], most of these studies composed of a limited numbers less than a hundred of side to end cases. We therefore conducted this study to determine short-term outcomes and oncologic clearance of side-to-end anastomosis after low anterior resection in rectal cancer patient.

Material and Method

Data sources and study design

After approval by the Siriraj Institutional Review Board (SIRB), we performed a retrospective patient chart review of patients diagnosed with rectal cancer. These patients underwent low anterior resection with side-to-end an astomosis in the Colorectal Surgery Unit, Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University between July 2007 and April 2010.

Inclusion and exclusion criteria

Rectal cancer was defined as a tumor located within 15 cm above the anal verge which could be classified intraoperatively into above, astride and below the peritoneal reflection. Inclusion criteria were: 1) Patients who underwent low anterior resection with side-to-end anastomosis, 2) elective surgery, and 3) rectal adenocarcinoma confirmed by pathological examination. Patients who underwent emergency surgery, surgery for recurrent cancer, synchronous cancer and surgery for metachronous cancer were excluded.

Perioperative parameters

Preoperative parameters were collected including age, gender, body mass index (BMI), co-morbid diseases, previous surgical history, symptoms at presentation, preoperative investigation and imaging, carcinoembryonic antigen (CEA) level, American Society of Anesthesiologist (ASA) classification. Intraoperative findings and postoperative results were also reported including mortality and morbidities, hospital stay, time of diet resumption, re-admission rate, re-operation rate, pathological staging and oncologic clearance results.

Statistical analysis

Qualitative data were summarized using frequencies and percent, while quantitative data were summarized using means, median, standard deviations, and interquartile ranges. Analysis was performed using SPSS for Windows version 17.0 (Chicago, Illinois).

Results

Demographic data and preoperative parameters

One hundred and thirteen patients were included. The mean age of the patients was sixty and there were no differences between the male and female gender (50.4% vs. 49.6%). The mean body mass index was 23.4 kg/m^2. Half of patients had co-morbid diseases (56.6%) which included hyperlipidemia, diabetes mellitus and hypertension. Most patients were ASA Class I and Class II (25.7% and 56.6%). Some of them had taken medications which had an antiplatelet or anticoagulation function such as Aspirin and Warfarin (12.4% and 0.9% respectively). One third of patients had a history of previous abdominal surgery while 11.5 percent had a history of colorectal cancer in their family (Table 1).

Preoperative symptoms and investigations

Patients presented with many symptoms such as mucous bloody stool, tenesmus, change of stool caliber etc. Seventy-six point one percent of tumors could be palpated by digital rectal examination. Neither supraclavicular lymph node nor abdominal mass was palpable. In terms of preoperative investigation, a colonoscopy was primarily performed to confirm the diagnosis, localize the tumor and obtain tissue biopsy. While 77 percent of cases used a computerized tomography (CT) scan to assess preoperative staging. The median CEA level was 4.78 ng/ml. Six patients received preoperative neoadjuvant chemo-radiation while one patient received preoperative radiation alone. Nine patients (8%) needed a preoperative blood transfusion (Table 2 and 3).

Intraoperative findings and details

Most tumors were located at or below the peritoneal reflection (72.5%). En-bloc other organ

Table 1. Demographic and preoperative data

	n = 113 (%)
Age (years)	60±12.5*
Gender	
Male	57 (50.4)
Female	56 (49.6)
BMI (kg/m^2)	23.4±3.5*
ASA classification	
I	29 (25.7)
II	64 (56.6)
III	17 (15)
IV	1 (0.9)
Co-morbidity	64 (56.6)
Hypertension	38 (33.3)
Diabetes	20 (17.7)
Dyslipidemia	14 (12.2)
Coronary artery disease	6 (5.3)
Valvular heart disease	4 (3.5%)
Arrhythmia	3 (2.7%)
Chronic obstructive pulmonary disease (COPD)	3 (2.7%)
Chronic kidney disease	2 (1.8%)
Family history of colorectal cancer	13 (11.5%)
History of previous abdominal surgery	38 (33.6%)
Preoperative medication	
Aspirin	14 (12.4%)
Antiplatelet	2 (1.8%)
Warfarin	1 (0.9%)
NSAIDs	1 (0.9%)

* Mean ± SD
BMI = Body mass index; ASA = American Society of Anesthesiologist

Table 2. Presenting symptoms and signs

	n = 113 (%)
Symptoms	
Bloody stool	88 (77.9)
Mucus stool	62 (54.9)
Change of stool caliber	53 (46.9)
Constipation	42 (37.2)
Diarrhea	31 (27.4)
Tenesmus	35 (31.0)
Abdominal pain	16 (14.2)
Loss of appetite	17 (15.0)
Weight loss	15 (13.3)
Palpable rectal mass	86 (76.1)
Tumor distance above anal verge (cm)	7 (6 to 10)*

* Median (interquartile range)

Table 3. Preoperative investigation and intervention

	n = 113 (%)
Investigation	
Colonoscopy	87 (77.0)
Sigmoidoscopy	28 (24.8)
DCBE	21 (18.6)
Imaging	
CT scan	83 (73.5)
Ultrasonography	30 (26.5)
MRI	3 (2.7)
CEA level (ng/ml)	4.78 (2.4 to 15.9)*
Preoperative blood transfusion	9 (8.0%)
Preoperative radiotherapy	7 (6.2%)
Preoperative chemotherapy	6 (5.3%)

* Median (interquartile range)
DCBE = Double contrast barium enema; CEA = Carcino-embryonic antigen

resections were performed in seven patients (6.2%). A double staple technique was commonly used to perform side-to-end anastomosis. Coloanal anastomosis was performed in 11.5 percent of the patients. An air leak test was performed in 44.2 percent of patients and drain placement was performed in less than half of the patients (45%). A tube drain or Jackson-Pratt drain were commonly used. Protective ostomies were only performed in 11 cases (9.7%). Most surgeons preferred loop ileostomy rather than loop transverse colostomy (7.1% vs. 3.5%) for a protective stoma. The mean operative time was 250 minutes and the average blood loss was 560 milliliters. One fourth of them (26%) required intraoperative blood transfusions (Table 4).

Short-term outcomes

There was one death from aspiration pneumonia with acute respiratory distress syndrome (ARDS) and acute renal failure. Eleven percent of patients required postoperative blood transfusions and 14 percent of them were monitored in the Intensive Care Unit. The median time to solid diet was 110 hours after surgery, and the median hospital stay was 11 days (Table 5).

The overall complication rate was 38.9%, including superficial surgical site infection (13.3%), urinary retention (9.7%), anastomosis leakage (6.2%), collection (5.3%), and postoperative ileus (4.4%). Regarding anastomosis leakage which was 6.2 percent, all patients had no protective stoma and no

Table 4. Intraoperative findings and details

	n = 113 (%)
Location of tumor	
Above peritoneal reflection	31 (27.4%)
Astride peritoneal reflection	37 (32.7%)
Below peritoneal reflection	45 (39.8%)
En-bloc organ resection	
Urinary bladder	2 (1.8%)
Salpingo-oophorectomy	2 (1.8%)
TAH with SO	2 (1.8%)
Type of anastomosis	
Colorectal	100 (88.5%)
Coloanal	13 (11.5%)
Technique of anastomosis	
Double staple	87 (77%)
Hand-sewn	23 (20.4%)
Single staple	3 (2.7%)
Air leak test	50 (44.2%)
Drain placement	51 (45.1%)
Tube	26 (23%)
Jackson-Pratt	24 (21.2%)
Penrose	1 (0.9%)
Protective ostomy	12 (10.6%)
Loop ileostomy	8 (7.1%)
Loop transverse colostomy	4 (3.5%)
Operative time (min)	249.1±92.6*
Estimated blood loss (mL)	561.1±462.6*
Blood transfusion	29 (25.7%)

* Mean ± SD
TAH with SO = Transabdominal hysterectomy with salpingo-oophorectomy

Table 5. Postoperative short-term outcomes

	n = 113 (%)
30-day mortality	1 (0.9)
Overall complication	44 (38.9)
Superficial surgical site infection	15 (13.3)
Urinary retention	11 (9.7)
Anastomosis leakage	7 (6.2)
Intraabdominal collection	6 (5.3)
Postoperative bowel ileus	5 (4.4)
Perioperative myocardial infarction	2 (1.8)
Atelectasis	2 (1.8)
Urinary Tract Infection	2 (1.8)
Cerebrovascular accident (CVA)	1 (0.9)
Pneumonia	1 (0.9)
Wound disruption	1 (0.9)
Postoperative ICU stay	16 (14.2)
Blood transfusion	13 (11.5)
Time to water sipping (hours)	66 (48 to 72)*
Time to liquid diet resumption (hours)	96 (96 to 120)*
Time to solid diet resumption (hours)	110 (90 to 120)*
Hospital stay (days)	11 (9.8 to 13)*

* Median (interquartile range)

preoperative adjuvant chemo-radiation. There was equal distribution of tumor locations above, at and below the peritoneal reflection. Most of them needed diversion and drainage. One patient underwent a dismantling anastomosis and another patient was successfully managed conservatively (Table 6).

Pathological staging and results

Most of the tumors were Stages II and III (25.7% and 47.9% respectively). One third of the specimens had both angiolymphatic and perineural invasion. Half of patients had positive lymph node metastasis. The median number of harvested lymph nodes was 18. The average proximal resected margin was 18 cm while the average distal resected margin was 2.6 cm. All resection margins were free of tumor in 93.8%, the circumferential margin was positive in 4.4%, and the distal margin was positive in 1.7% (Tables 7 and 8).

Discussion

In the present study, the patient demographic data, presenting symptoms and signs, preoperative parameters were similar to other studies[11-13]. Most of rectal cancers in the present study were locally advanced tumors with Stage II and Stage III disease. Preoperative neoadjuvant chemo-radiation cases in the present study were approximately six percent. This was according to the strategy of treatment in the authors' institute which might be different from treatment strategies in a Western country. The authors preferred to perform the surgical procedure followed by postoperative adjuvant chemo-radiation when the tumor was not close to the mesorectal fascia after evaluation by preoperative imaging such as computerized tomography scan or magnetic resonance imaging of the pelvis. If the tumor was bulky or close to the mesorectal fascia or with a high possibility of gaining a R1 or R2 positive margin, the authors selected preoperative neoadjuvant chemo-radiation in these cases.

To perform anastomosis after low anterior resection, there are several methods of reconstructing a neo-rectum to avoid an anterior resection syndrome. A colonic J-pouch or a transverse coloplasty were two common procedures that were created. Lazorthes et al and Parc et al independently described the construction

Table 6. Anastomosis leakage cases

Case	Tumor location	Intervention
1	Above peritoneal reflection	Loop ileostomy and drainage
2	Below peritoneal reflection	Loop ileostomy and drainage
3	Below peritoneal reflection	Loop transverse colostomy and drainage
4	Above peritoneal reflection	Loop transverse colostomy and drainage
5	Below peritoneal reflection	Loop transverse colostomy and percutaneous drainage
6	Below peritoneal reflection	Dismantle anastomosis
7	At peritoneal reflection	Conservative treatment

Table 7. Pathological results

	n = 113 (%)
Depth of tumor invasion	
Invade submucosa	6 (5.3)
Invade muscularispropria	25 (22.1)
Invade into perirectal tissue	78 (69.0)
Invade or adhere other organs or structures	4 (3.5)
Number of metastasis lymph nodes	
No regional lymph node metastasis	53 (46.9)
Metastasis in 1 regional lymph node	11 (9.7)
Metastasis in 2-3 regional lymph nodes	12 (10.6)
Metastasis in 4-6 regional lymph nodes	15 (13.3)
Metastasis in 7 or more regional lymph nodes	22 (19.5)
Vascular invasion	37 (32.7)
Lymphatic invasion	41 (36.3)
Perineural invasion	27 (23.9)
Proximal resected margin (cm)*	13 ± 7[a]
Distal resected margin (cm)*	2.6 ± 1.5[a]
Resected surgical margin	
All free	106 (93.8)
Positive circumferential margin	5 (4.4)
Positive proximal margin	0 (0)
Positive distal margin	2 (1.7)
Total number of harvested lymph nodes	18 (14-25)[b]

[a] Mean $\pm$ SD; [b] Median (interquartile range)
* Measured from fresh specimen

of a colonic J-pouch (CJP) in 1986[14,15], while transverse coloplasty (TCP) was first described by Z'Graggen et al in a porcine model in 1999[16,17] and was subsequently introduced into clinical practice[18,19]. Nevertheless, most surgeons in the authors' institute prefer performing side-to-end or Baker's anastomosis because this technique has several advantages such as: 1) It is simple and can be performed faster than CJP. 2) It needs less colonic length with comparable functional outcomes. 3) The blood supply of side-to-end anastomosis is not compromised. 4) It could be used in a narrow pelvic cavity patient as in TCP. Recently, a systematic review reported no differences in bowel function outcomes among side-to-end, colonic J-pouch, and transverse coloplasty[10]. Furthermore, Hallbook et al reported no unaffected blood flow at the site of a side-to-end anastomosis[9].

Short-term outcomes of anastomosis reconstruction after low anterior resection can be measured in several ways. These include morbidities, mortality and hospital stay. Anastomosis leakage seems to be an important measurable morbidity. Leakage of anastomosis could vary from 2.8 to 12 percent[12,13,20-23]. Anastomosis leakage rate after reconstruction with side-to-end type in the present study was therefore acceptable and comparable to other types of reconstruction. Although the authors could not demonstrate factors that influenced anastomosis leakage in the present study due to the small number of anastomosis patients with leakage. Several factors have been widely studied for this morbidity for example the level of anastomosis, use of pelvic drain and protective stoma. Most studies reported that the level of anastomosis within 6 cm. above the anal verge is a major risk factor. However, some studies found that presence of pelvic drains and defunctioning the stoma were associated with lower anastomosis leakage[12,13,20-23].

Other common complications were also evaluated in the present study such as superficial surgical site infection (13.3%) and urinary retention (9.7%). Postoperative urinary retention rate after low anterior resection is rarely reported. The result of the present study was comparable to the result reported by Zaheer et al which was16.3 percent[24]. This complication might be due to dissection close to the pelvic autonomic nerve due to a large bulky tumor. It seems that urinary retention in laparoscopic low anterior

Table 8. Pathological TNM staging*

Stage	%	T	N	M	n = 113 (%)
I	21.2	T1	N0	M0	6 (5.3)
		T2	N0	M0	18 (15.9)
IIA		T3	N0	M0	28 (24.8)
IIB	25.7	T4a	N0	M0	-
IIC		T4b	N0	M0	1 (0.9)
IIIA		T1-T2	N1/N1c	M0	3 (2.7)
		T1	N2a	M0	-
IIIB		T3-T4a	N1/N1c	M0	19 (16.8)
	47.8	T2-T3	N2a	M0	13 (11.5)
		T1-T2	N2b	M0	3 (2.7)
IIIC		T4a	N2a	M0	-
		T3-T4a	N2b	M0	14 (12.4)
		T4b	N1-N2	M0	2 (1.8)
IVA	5.3	AnyT	AnyN	M1a	4 (3.5)
IVB		AnyT	AnyN	M1b	2 (1.8)

* TNM staging from the seventh edition of the American Joint Committee on Cancer (AJCC) cancer staging manual

resection has been reported to be as low as 3 to 3.8 percent[25,26].

There were some limitations of the present study. First, it was not a comparative study with other types of neo-rectum reconstruction such as colonic J pouch and transverse coloplasty. Second, the authors did not report long-term oncologic and functional outcomes in the present study. Finally, the predictive factors of anastomotic leakage were not stated.

Conclusion

Short-term outcomes and oncologic clearance of low anterior resection with side-to-end anastomosis were comparable to reported outcomes in other studies. Long-term oncologic and functional outcomes need to be studied further.

What is already known on this topic?

Low anterior resection is the preferable surgical treatment in rectal cancer patients with acceptable short term outcomes and oncologic clearance as well as its sphincter saving benefit.

What this study adds?

Side-to-end anastomosis technique does not deteriorate short term perioperative and oncologic results. Low anterior resection with reconstruction by this technique is a suitable surgical treatment in rectal cancer patients.

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Potential conflicts of interest

None.

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ผลการรักษาระยะสั้นในผู้ป่วยมะเร็งลำไส้ตรงโดยการผ่าตัด Low Anterior Resection และต่อลำไส้แบบ Side-to-End

ร่มเย็น จิตมุ่งงาน, เชิดศักดิ์ ไอรมณีรัตน์, วิรุณ บุญนุช, ดรินทร์ โล่ห์สิริวัฒน์, วรมินทร์ เหรียญสุวรรณ

ภูมิหลัง: การผ่าตัด Low Anterior Resection เป็นการผ่าตัดทางเลือกหนึ่งที่ทำให้บรรลุทั้งการตัดเนื้องอกออก และสามารถเก็บหูรูดได้ ในผู้ป่วยมะเร็งลำไส้ตรง ถึงแม้ผลลัพธ์ของการต่อลำไส้แบบ side-to-end หลังการผ่าตัด Low Anterior resection จะเป็นที่ยอมรับแต่การศึกษาส่วนใหญ่มักเป็นการศึกษาในกลุ่มประชากรขนาดเล็กและการศึกษาในคนไทยยังมีจำกัด ดังนั้นผู้นิพนธ์ได้ดำเนินการวิจัยนี้เพื่อศึกษาผลการรักษาระยะสั้นในผู้ป่วยมะเร็งลำไส้ตรงโดยการผ่าตัด Low Anterior Resection และต่อลำไส้แบบ side-to-end

วัสดุและวิธีการ: เวชระเบียนผู้ป่วยมะเร็งลำไส้ตรงที่ได้รับการผ่าตัด Low Anterior Resection และต่อลำไส้แบบ side-to-end ในหน่วยศัลยศาสตร์ลำไส้ใหญ่และทวารหนัก ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล ระหว่าง เดือนกรกฎาคม พ.ศ. 2550 ถึง เดือนเมษายน พ.ศ. 2553 ได้รับการทบทวนแบบย้อนหลัง สถิติประชากร ข้อมูลระหว่างการผ่าตัดและผลลัพธ์ระยะสั้นหลังการผ่าตัดของผู้ป่วยในกลุ่มประชากรของการวิจัยนี้ได้รับการวิเคราะห์

ผลการศึกษา: ผู้ป่วยของการวิจัยนี้มีทั้งหมด 113 รายมีอายุเฉลี่ย 60 ปี เป็นชาย 57 ราย (ร้อยละ 50.4) เป็นหญิง 56 ราย (ร้อยละ 49.6) ผู้ป่วยร้อยละ 6 ได้รับเคมีบำบัดและการฉายรังสีรักษาก่อนการผ่าตัด ระยะเฉลี่ยของก้อนมะเร็ง ห่างจากปากทวาร 6.7 เซนติเมตร เมื่อพิจารณาตำแหน่งของก้อนมะเร็งกับ peritoneal reflection พบว่าผู้ป่วย 31 ราย (ร้อยละ 27.4) อยู่สูงกว่า ผู้ป่วย 37 ราย (ร้อยละ 32.7) อยู่ที่ peritoneal reflection และผู้ป่วย 45 ราย (ร้อยละ 39.8) อยู่ต่ำกว่าการตรวจทางพยาธิวิทยาพบว่า ชิ้นเนื้อที่ผ่าตัดออกมาเป็นเนื้องอกระยะ T3 ร้อยละ 67.3 และครึ่งหนึ่งของผู้ป่วยมีมะเร็งกระจายไปยังต่อมน้ำเหลืองโดยจำนวนต่อมน้ำเหลืองทั้งหมดที่ตัดออกมาได้มีค่ามัธยฐานที่ 18 ต่อม ขอบเขตของการผ่าตัดตรวจพบมะเร็งในระดับจุลทรรศน์ร้อยละ 6.1 ภาวะแทรกซ้อนทั้งหมดหลังผ่าตัดพบได้ร้อยละ 38.9 โดยมีอัตราการเกิดรอยต่อลำไส้รั่วร้อยละ 6.2 และมีผู้ป่วยเพียงหนึ่งรายเสียชีวิตหลังผ่าตัด ระยะเวลาที่กลับมารับประทานอาหารชนิดปกติ 110 ชั่วโมงและค่ามัธยฐานของจำนวนวันที่อยู่ในโรงพยาบาลคือ 11 วัน

สรุป: ผลการรักษาระยะสั้นรวมถึงการตัดมะเร็งออกได้หมดในผู้ป่วยมะเร็งลำไส้ตรงโดยการผ่าตัด Low Anterior Resection และต่อลำไส้แบบ Side-to-End ในการศึกษานี้เทียบเท่ากับรายงานในการศึกษาอื่น อย่างไรก็ตามผลการรักษาในระยะยาวและการขับถ่ายอุจจาระหลังการผ่าตัดยังคงต้องติดตามต่อไปจากงานวิจัยในภายภาคหน้า