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第三十卷第三期

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Original Article

A Comparative Study of Short-term Clinical Outcome of Robotic vs. Laparoscopic Surgery for Rectal Cancer

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Key Words

Robotic;

Laparoscopic;

Rectal cancer;

Outcome

Purpose. In this study, we aimed to compare surgical parameters and short-term postoperative clinical outcomes of robotic vs. laparoscopic rectal cancer surgery.

Methods. From May 2016 to Nov 2018, we retrospectively reviewed 46 patients who underwent robotic and laparoscopic rectal cancer surgery at our institution by a single surgeon. Patient characteristics and perioperative demographic data were collected and short-term clinical outcomes were compared, including TNM stage, preoperative chemoradiotherapy, postoperative radiotherapy, surgical parameters and postoperative outcomes.

Results. Of 46 total patients, 21 underwent robotic surgery and the remaining 25 underwent laparoscopic rectal cancer surgery. There was no significant difference in patient characteristics between surgical groups. Mean operative time was longer in robotic surgery than laparoscopic surgery (robotic: 301.4 vs. laparoscopic: 206 min, $p < 0.001$); mean estimated blood loss was not statistically different (robotic: 101.9 vs. 72.8 ml, $p = 0.334$). No significant difference was detected with regard to pathological outcome or postoperative complications.

Conclusion. Robotic rectal cancer surgery had greater operative time but made no difference in postoperative short-term complication and outcome compared with laparoscopic rectal cancer surgery, which offers another safe, operative method.

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According to the 2017 Statistics of Causes of Death from Ministry of Health and Welfare of Taiwan, malignant neoplasms were still the major cause of death over the past four decades, with a standardized death rate of colorectal cancer of 14%;¹ the proportion of colorectal cancer incidence in 2015 was 43%.² For those who did not have locally advanced colon cancer, surgical excision was the optimal treatment according to clinical staging. Minimally inva-

sive surgery has an advantage over conventional open surgery with its smaller wound size, reduced postoperative pain, and shorter hospitalization time. Several studies have shown that laparoscopic resection had fewer complications compared to open surgery.³⁻⁷ Rectal cancer surgery has its own technical challenges, due to the limitation of the pelvic operation field and difficulty in instrument application. Robotic rectal surgery (RRS) has the same benefits as laparoscopy

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with three-dimensional vision and precise instrument application, a clearer operation image experience, and similar short-term perioperative outcomes compare with laparoscopic rectal surgery (LRS). However, the increased cost and longer operation time has been cited as disadvantages of RRS.^{14,17-19,30} The aim of this study was to compare robotic to laparoscopic rectal cancer surgery performed by a single surgeon at a single-center hospital with regard to short-term clinical outcomes.

Materials and Methods

Patient selection

This was a retrospective study of data collected from the medical database of Changhua Christian Hospital between May 2016 and Nov 2018. We studied a total of 46 patients with rectal cancer underwent primary RRS and LRS by a single experienced surgeon (experience with > 100 laparoscopic surgeries). Among them, 21 underwent RRS and the remaining 25 underwent LRS. The operation method included low anterior resection, abdomino-perineal resection, and Hartmann's operation, depending on the location of the tumor. Patients who had recurrent cancer, multiple-organ cancer, or multiple procedures were excluded from our study. The preoperative work-up included colonoscopy, preoperative carcinoembryonic antigen, and imaging study with abdomen computed tomography scan, positron emission tomography, or magnetic resonance imaging. Patients with advanced clinical stage received neoadjuvant chemoradiation (5,600 cGy administered in 28 fractions with 5-fluorouracil based chemotherapy) were followed up by surgical resection within 8 weeks. Patients were staged according to the American Joint Committee on Cancer staging manual (7th edition). Two groups based on robotic or laparoscopic surgery were compared for perioperative short-term outcome.

We collected data of patient characteristics, including sex, age, body mass index, comorbidities (hypertension, diabetes mellitus, end stage renal disease, and coronary artery disease), preoperative concurrent

chemoradiotherapy (CCRT), postoperative radiotherapy (RT), diverting stoma, pre-operation carcinoembryonic antigen (CEA), and pre-operation carbohydrate antigen 19-9 (CA19-9). Patients whose circumferential resection margin (CRM) was involved with the tumor were treated with postoperative radiotherapy. The operation outcomes included operation method (low anterior resection, abdomino-perineal resection, and Hartmann's procedure) performed according to tumor location, estimated blood loss, number of lymph node harvested, diverting stoma, CRM positive, tumor size, total hospital stay, day of intake, and readmission within 30 days. Operative time was defined as the duration of time between the first skin incision and closure. Tumor location was defined as the distance of the tumor from the anal verge and classified into upper (11-15 cm), middle (6-10 cm), and lower (0-5 cm). Pathological outcomes were defined with TNM stage, according to the American Joint Committee on Cancer staging manual (7th edition). Surgical complications were anastomosis leakage (major or minor), ileus, wound infection, chylous leakage, and mortality. Anastomosis leakage was defined as bowel content detected through a drainage tube or wound, or via imaging study. Minor leakage was defined as anastomosis leakage and was treated with nothing by mouth, antibiotics, drainage, and peripheral parenteral nutrition without surgical intervention; major leakage was defined as anastomotic leakage that required surgical intervention. Ileus was defined as no flatus or no stool passage with abdominal distension or vomiting persisting on the fifth postoperative day and the need for nasogastric tube decompression with peripheral parenteral nutrition treatment.

Surgical technique

All RRS and LRS were performed by a single experienced surgeon (over 100 laparoscopic surgeries) at our institution. The RRS was performed using the da Vinci Si Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) to perform surgery. The initial procedure to create a pneumoperitoneum was similar between the two groups with the open Hasson technique. The RRS had one 12-mm supra-umbilical cam-

era port, another four 8-mm robotic working ports over the epigastrium, right flank, left flank, and suprapubic region, and one 5-mm assistant port over right flank. The LRS had one 12-mm supra-umbilical camera port, two working ports (5-mm and 12-mm) over the right flank, and one 5-mm assistant port over the left flank. The technique to mobilize the colon, pelvic dissection, rectal anastomosis, and ileostomy creation was similar between groups. Hem-o-lok was used for inferior mesenteric artery ligation in RRS and endoscopic linear stapler or endoscopic hemoclip was applied during LRS. Energy device with LigaSure™ was used only in LRS.

Statistical analysis

Categorical variables were recorded as number of cases and percentage, whereas continuous variables were showed as mean \pm standard deviation. The chi-squared test was used to compare categorical vari-

ables and Fisher's exact test was used when the minimum expected value was less than five. Continuous variables were compared by independent samples Student's *t*-test or the Mann-Whitney *U* test. A two-sided *p* value < 0.05 was considered statistically significant. All analyzes were performed using SPSS statistical software version 12 (SPSS Inc, Chicago, IL, USA).

Results

In this study, a total of 46 patients underwent minimally invasive surgery for rectal cancer, of which 21 underwent RRS and 25 underwent LRS. Demographic characteristics are shown in Table 1. No significant differences were found with regard to sex, age, body mass index, hypertension, diabetes mellitus, end stage renal disease and coronary artery disease, preoperative CCRT, postoperative RT. There were also no significant differences in the preoperative CEA, pre-

Table 1. Patient characteristics

	Robotic (n = 21)	Laparoscopic (n = 25)	<i>p</i> value
Sex			0.22
Male	15 (72%)	14 (56%)	
Female	6 (28%)	11 (44%)	
Age			0.569
< 65 y	13 (62%)	15 (60%)	
≥ 65 y	8 (38%)	10 (40%)	
Body mass index (kg/m ²)	24.8 \pm 4.1	22.7 \pm 4.5	0.108
Comorbidities			
Hypertension	11 (52%)	12 (48%)	0.5
Diabetes mellitus	5 (24%)	1 (4%)	0.079
End stage renal disease	1 (5%)	1 (4%)	1
Coronary artery disease	1 (5%)	1 (4%)	1
Pre-operation CCRT	5 (24%)	7 (28%)	0.508
Post-operation RT	1 (5%)	1 (4%)	1
Pre-operation CEA (ng/mL)	5.7 \pm 4.7	34.9 \pm 72.3	0.066
Pre-operation CA19-9 (U/mL)	24.8 \pm 38.4	533.9 \pm 2235.2	0.773
TNM Stage			0.152
0	3 (14%)	2 (8%)	
I	8 (38%)	3 (12%)	
II	3 (14%)	5 (20%)	
III	7 (34%)	12 (48%)	
IV	0	3 (12%)	

Data are represented as mean \pm standard deviation and (ratio).

CCRT: concurrent chemoradiotherapy; RT: radiotherapy; CEA: carcinoembryonic antigen; CA19-9: carbohydrate antigen 19-9.

According to AJCC/UICC TNM staging.

operation CA 19-9. More patients who underwent LRS had advanced stage (\geq stage III; 15 vs. 7; $p = 0.152$), but this was not significantly different.

Perioperative outcomes

The perioperative outcomes showed in Table 2. The operative method ($p = 0.198$) was performed as low anterior resection (RRS: 20 vs. LRS: 19 patient), abdomino-perineal resection (RRS: 1 vs. LRS: 5 patient) and Hartmann's procedure (RRS: 0 vs. LRS: 1 patient), but no significant difference between was found between groups. Operative time was significantly longer in RRS than in LRS (RRS: 301.4 vs. LRS: 206 mins; $p < 0.001$). Estimated blood loss was similar (RRS: 101.9 vs. LRS: 72.8 ml; $p = 0.334$). There were no significant difference with regard to diverting stoma (RRS: 16 vs. LRS: 17; $p = 0.539$), lymph node retrieval (RRS: 17.6 vs. LRS: 17.7; $p = 0.973$), tumor size (RRS: 35.21 vs. LRS: 30 cm³; $p = 0.707$), CRM positive (RRS: 1 vs. LRS: 1; $p = 1$), total hospital stay (RRS: 10.8 vs. LRS: 10.5 days; $p = 0.858$), day of intake (RRS: 3.1 vs. LRS: 2.2 days; $p = 0.755$).

Table 2. Operation outcomes

	Robotic (n = 21)	Laparoscopic (n = 25)	<i>p</i> value
Operation method			0.198
Low anterior resection	20 (95%)	19 (76%)	
APR	1 (5%)	5 (20%)	
Hartmann's procedure	0	1 (4%)	
Operative time (mins)	301.4 \pm 56.9	206 \pm 63.5	< 0.001
Estimated blood loss (ml)	101.9 \pm 127.3	72.8 \pm 71.2	0.334
Diverting stoma	16 (76%)	17 (68%)	0.539
Lymph node retrieval	17.6 \pm 7.8	17.7 \pm 11.4	0.973
Tumor size (cm ³)	35.21 \pm 43.5	30 \pm 47.5	0.707
Tumor location (cm)			0.742
Upper (11-15 cm)	4 (19%)	5 (20%)	
Middle (6-10 cm)	6 (29%)	10 (40%)	
Low (0-5 cm)	11 (52%)	10 (40%)	
CRM positive	1 (5%)	1 (4%)	1
Total hospital stay (day)	10.8 \pm 4.8	10.5 \pm 4.3	0.858
Day of intake	3.1 \pm 3.7	2.2 \pm 0.7	0.755

Data are represented as mean \pm standard deviation and ratio.

CRM: circumferential resection margin; APR: abdomino-perineal resection.

Postoperative complications are showed in Table 3. There were no significant difference in postoperative complications ($p = 0.611$), including minor leakage (RRS: 0 vs. LRS: 2), major leakage (RRS: 1 vs. LRS: 1) ($p = 0.614$), ileus (RRS: 2 vs. LRS: 5; $p = 0.428$), wound infection (RRS: 2 vs. LRS: 2; $p = 1$), chylous leakage (RRS: 2 vs. LRS: 1; $p = 0.585$), mortality (RRS: 1 vs. LRS: 0; $p = 0.457$), readmission within 30 days (RRS: 1 vs. LRS: 3; $p = 0.614$) between RRS and LRS. One patient with major leakage in RRS underwent diverting stoma, and one patient in LRS suffered from ileostomy obstruction with colon anastomosis site necrosis and subsequently underwent ileostomy revision and drainage of intra-abdominal abscess. One patient with end stage renal disease in RRS encountered mortality because of pneumonia and pulmonary edema. One patient in RRS encountered iatrogenic bladder injury because of adhesion. One patient in RRS had to be readmitted within 30 days because of partial intestinal obstruction, high output stoma with dehydration, and electrolyte imbalance. Two patients in LRS were readmitted due to urinary tract infection and persistent ileus.

Discussion

The aim of this study was to compare short-term outcome of RRS with LRS. In our study, all surgery were performed by single surgeon, operative time was significant longer in RRS than LRS. There were no significant differences in demographic characteristics, perioperative outcomes, or complications between the

Table 3. Postoperative complications

	Robotic (n = 21)	Laparoscopic (n = 25)	<i>p</i> value
Complication	6 (28.6%)	7 (28%)	0.611
Leakage	1 (4.8%)	3 (12%)	0.614
Minor	0	2 (8%) [†]	
Major	1 (4.8%)*	1 (4%)*	
Ileus	2 (9.5%)	5 (20%)	0.428
Wound infection	2 (9.5%)	2 (8%)	1
Chylous leakage	2 (9.5%)	1 (4%)	0.585
Mortality	1 (4.8%)	0	0.457
Readmission within 30 days	1 (5%)	2 (8%)	1

RRS and LRS groups.

Several studies have reported that robotic surgery operative time was longer than laparoscopic surgery.⁸⁻¹² Min et al. studied 278 rectal cancer patients who underwent robotic surgery among 1029 total patients, finding that robotic surgery had a longer operative time than the laparoscopic group (361.6 ± 91.9 vs. 272.4 ± 83.8 mins; $p < 0.001$)¹³ similar with our study. In our study, the two groups had the same procedure after distal rectum transection and we determined two factors which accounted for the difference in operative time. First was the robotic instrument docking times, with the main factor being a lack of energy source device with LigaSureTM blunt tip laparoscopic sealer in RRS; this added time to the dissection with Da Vinci Maryland bipolar forceps. The other factor was the different method used for inferior mesenteric artery ligation; RRS used Hem-o-lok was used in RRS and LRS utilized the endoscopic hemoclip or endoscopic linear cutter stapler. The estimated blood loss was similar between two groups, consistent with most previous studies. Interestingly, some studies have actually reported less blood loss in robotic surgery.¹⁴⁻¹⁶

Our finding of similar clinical and pathological outcomes between RRS and LRS are similar with previous reports.^{11-14,17-20} Four patients in the RRS group and two patients in LRS did not have diverting stoma performed according to the surgeon's decision regarding location, tension, and perfusion over the anastomosis site. Those who did not have diverting stoma underwent preoperative CCRT that had a greater risk of anastomosis leakage.^{21,22} One patient in RRS encountered major leakage without diverting stoma and received a second operation with diverting stoma. One patient with end stage renal disease occurred mortality within postoperative 30 days in RRS encountered with pneumonia and pulmonary edema, but the family refused advanced respiratory intubation support. There are several meta-analyses reporting that robotic surgery had a lower conversion rate to open surgery compared to laparoscopy.²³⁻²⁹ Seon et al. reported robotic group had a shorter time to first flatus and better recovery in voiding and sexual function.²⁵ Binghong et al. reported that the positive rate of CRMs ($p = 0.04$) and incidence of erectile dysfunction ($p =$

0.002) were lower in the robotic group compared with the laparoscopic group.²⁹ However, cost analysis in several studies showed that robotic surgery was more expensive than laparoscopic surgery.^{14,17-19,30}

There were several limitations in our study which warrant discussion. First, this was a retrospective study without randomization and with a small sample size. Second, all surgeries were performed by a single surgeon, which may have led to a selection bias. Third, the oncological outcomes were not analyzed; long-term oncological outcomes need further analysis.

Conclusions

Robotic rectal cancer surgery had longer operative time but no significant difference in postoperative short-term complication or outcomes compared with laparoscopic rectal cancer surgery, offering another safe operative method.

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References

1. Ministry of Health and Welfare. Statistics cause of death statistics 2017. <https://www.mohw.gov.tw/dl-46137-afa32e57-3b43-40b7-8a83-26ff3568f3bf.html>.
2. Ministry of Health and Welfare. Leading cancer incidence rate 2015. <https://dep.mohw.gov.tw/DOS/cp-1720-7336-113.html>.
3. Chen K, Cao GD, Chen B, et al. Laparoscopic versus open surgery for rectal cancer: a meta-analysis of classic randomized controlled trials and high-quality nonrandomized studies in the last 5 years. *Int J Surg* 2017;39:1-10.
4. Martínez-Pérez A, Clotilde Carra M, Brunetti F, et al. Pathologic outcomes of laparoscopic vs open mesorectal excision for rectal cancer: a systematic review and meta-analysis. *JAMA Surg* 2017;152(4):e165665.
5. Yamaguchi T, Konishi T, Kinugasa Y, et al. Laparoscopic versus open lateral lymph node dissection for locally advanced low rectal cancer: a subgroup analysis of a large multicenter cohort study in Japan. *Dis Colon Rectum* 2017;60(9):954-64.
6. Martínez-Pérez A, Carra MC, Brunetti F, de'Angelis N.

Short-term clinical outcomes of laparoscopic vs open rectal excision for rectal cancer: a systematic review and meta-analysis. *World J Gastroenterol* 2017;23(44):7906-16.

7. Fleshman J, Branda M, Sargent DJ, et al. Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes: The ACOSOG Z6051 Randomized Clinical Trial. *JAMA* 2015;314(13):1346-55.
8. Crolla RMPH, Mulder PG, van der Schelling GP. Does robotic rectal cancer surgery improve the results of experienced laparoscopic surgeons? An observational single institution study comparing 168 robotic assisted with 184 laparoscopic rectal resections. *Surg Endosc* 2018.
9. Hellan M, Ouellette J, Lagares-Garcia JA, et al. Robotic rectal cancer resection: a retrospective multicenter analysis. *Ann Surg Oncol* 2015;22(7):2151-8.
10. Jayne D, Pigazzi A, Marshall H3, et al. Effect of robotic-assisted vs conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer: The ROLARR Randomized Clinical Trial. *JAMA* 2017;318(16):1569-80.
11. Kwak JM, Kim SH, Kim J, et al. Robotic vs laparoscopic resection of rectal cancer: short-term outcomes of a case-control study. *Dis Colon Rectum* 2011;54(2):151-6.
12. Park JS, Choi GS, Lim KH, et al. Robotic-assisted versus laparoscopic surgery for low rectal cancer: case-matched analysis of short-term outcomes. *Ann Surg Oncol* 2010;17(12):3195-202.
13. Cho MS, Baek SJ, Hur H, et al. Short and long-term outcomes of robotic versus laparoscopic total mesorectal excision for rectal cancer: a case-matched retrospective study. *Medicine (Baltimore)* 2015;94(11):e522.
14. Ramji KM, Cleghorn MC, Josse JM, et al. Comparison of clinical and economic outcomes between robotic, laparoscopic, and open rectal cancer surgery: early experience at a tertiary care center. *Surg Endosc* 2016;30(4):1337-43.
15. Yamaguchi T, Kinugasa Y, Shiomi A, et al. Robotic-assisted vs. conventional laparoscopic surgery for rectal cancer: short-term outcomes at a single center. *Surg Today* 2016;46(8):957-62.
16. Park SY, Choi GS, Park JS, et al. Short-term clinical outcome of robot-assisted intersphincteric resection for low rectal cancer: a retrospective comparison with conventional laparoscopy. *Surg Endosc* 2013;27(1):48-55.
17. Morelli L, Guadagni S, Lorenzoni V, et al. Robot-assisted versus laparoscopic rectal resection for cancer in a single surgeon's experience: a cost analysis covering the initial 50 robotic cases with the da Vinci Si. *Int J Colorectal Dis* 2016;31(9):1639-48.
18. Baek JH, Pastor C, Pigazzi A. Robotic and laparoscopic total mesorectal excision for rectal cancer: a case-matched study. *Surg Endosc* 2011;25(2):521-5.
19. Ielpo B, Duran H, Diaz E, et al. Robotic versus laparoscopic surgery for rectal cancer: a comparative study of clinical outcomes and costs. *Int J Colorectal Dis* 2017;32(10):1423-9.
20. Yoo BE, Cho JS, Shin JW, et al. Robotic versus laparoscopic intersphincteric resection for low rectal cancer: comparison of the operative, oncological, and functional outcomes. *Ann Surg Oncol* 2015;22(4):1219-25.
21. Lim SB, Yu CS, Kim CW, et al. Late anastomotic leakage after low anterior resection in rectal cancer patients: clinical characteristics and predisposing factors. *Colorectal Dis* 2016;18(4):O135-40.
22. Lee WS, Yun SH, Roh YN, et al. Risk factors and clinical outcome for anastomotic leakage after total mesorectal excision for rectal cancer. *World J Surg* 2008;32(6):1124-9.
23. Lin S, Jiang HG, Chen ZH, et al. Meta-analysis of robotic and laparoscopic surgery for treatment of rectal cancer. *World J Gastroenterol* 2011;17(47):5214-20.
24. Trastulli S, Farinella E, Cirocchi R, et al. Robotic resection compared with laparoscopic rectal resection for cancer: systematic review and meta-analysis of short-term outcome. *Colorectal Dis* 2012;14(4):e134-56.
25. Lee SH, Lim S, Kim JH, Lee KY. Robotic versus conventional laparoscopic surgery for rectal cancer: systematic review and meta-analysis. *Ann Surg Treat Res* 2015;89(4):190-201.
26. Memon S, Heriot AG, Murphy DG, et al. Robotic versus laparoscopic proctectomy for rectal cancer: a meta-analysis. *Ann Surg Oncol* 2012;19(7):2095-101.
27. Valverde A, Goasguen N, Oberlin O, et al. Robotic versus laparoscopic rectal resection for sphincter-saving surgery: pathological and short-term outcomes in a single-center analysis of 130 consecutive patients. *Surg Endosc* 2017;31(10):4085-91.
28. Ielpo B, Caruso R, Quijano Y, et al. Robotic versus laparoscopic rectal resection: is there any real difference? A comparative single center study. *Int J Med Robot* 2014;10(3):300-5.
29. Xiong B, Ma L, Huang W, et al. Robotic versus laparoscopic total mesorectal excision for rectal cancer: a meta-analysis of eight studies. *J Gastrointest Surg* 2015;19(3):516-26.
30. Araujo SE, Seid VE, Klajner S. Robotic surgery for rectal cancer: current immediate clinical and oncological outcomes. *World J Gastroenterol* 2014;20(39):14359-70.

原 著

對於直腸癌使用機器人手臂輔助與腹腔鏡輔助手術兩者比較：短期經驗分享

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目的 對於機器人手臂輔助及腹腔鏡輔助手術切除直腸癌，術中與術後預後比較。

方法 自 2016 年 5 月至 2018 年 11 月，共 46 位直腸癌患者接受單一手術醫師進行機器人手臂及腹腔鏡手術的回顧性研究。

結果 共 46 位直腸癌患者納入研究，21 位施行機器人手臂輔助手術，25 位施行腹腔鏡輔助手術。平均手術時間機器人手臂組對比腹腔鏡組較長 (301.4 vs. 206 分鐘， $p < 0.001$)，術中出血量沒有顯著差異 (101.9 vs. 72.8 毫升， $p = 0.334$)。病患基本資料，合併症，術前腫瘤指數，術中淋巴結摘除數量，術後併發症，病理結果，住院天數，術後進食時間及術後 30 天內再住院率及死亡率兩組沒有差異。

結論 機器人手臂輔助直腸癌手術相較腹腔鏡手術的花費的手術時間較長，但對於術中及術後併發症及預後並無顯著差異，因此相較腹腔鏡手術，仍是一個安全的手術方式。

關鍵詞 機器人手臂、腹腔鏡、直腸癌、預後。

Original Article

The Risk Factors Associated with 30-day Readmission after Colorectal Surgery: A Single-institute Analysis

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Key Words

30-day readmission;
Colorectal surgery;
Preoperative factors;
Postoperative factors

Purpose. Unplanned readmission has a negative impact on health insurance costs, patient satisfaction, and clinical outcome. Readmission rates indicate surgical quality and quality of care. This study aimed to identify the risk factors that may affect the 30-day readmission after colorectal surgery.

Materials and Methods. This retrospective study included 440 patients who underwent colorectal surgery at Chang Gung Memorial Hospital Keelung Branch between January 2, 2013, and December 21, 2015. Patients who received combined operation such as hepatectomy or cystectomy during the index surgery were excluded. Readmission due to scheduled stage operation were also excluded. The chi-square test (for categorical variables) and Student *t* test (for continuous variables) were used for the analysis. Logistic regression analysis was used for single-variable and multivariable analyses. *p* values of < 0.05 indicated significance.

Results. Of the 440 patients, 340 were included in the analysis after applying the exclusion criteria, of whom 35 (10.2%) were readmitted within 30 days after index admission discharge. Although the comorbidities, high American Society of Anesthesiologist (ASA) classification, lower preoperative albumin level, previous cerebral vascular accident, and index admission with major complications had significant impacts on readmission in the single-variable analysis, only the postoperative major complications had a significant impact on readmission in the multivariate analysis.

Conclusions. Although patient-related factors have a less direct influence on readmission within 30 days after index admission discharge, this study may lead us to change the strategies for addressing the readmission rate by focusing on reducing the incidence of avoidable postoperative complications.

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Unplanned readmission is associated with decreased patient satisfaction, increased health cost, and negative impact on clinical outcomes. In addition, readmission rates also represent medical and surgical qualities in our facility.

Among patients who underwent colorectal sur-

gery, readmission rates were estimated to range from 9% to 25%.¹ Previously reported risk factors are inconsistent among different countries, races, demographics, and perioperative factors.² In this study, our primary goal was to identify the factors associated with hospital readmission after colorectal surgery.

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The secondary goal of this study was to generate strategies to prevent readmission after colorectal surgery.

Materials and Methods

Patients

This study was approved by the institutional review board (IRB No. 201601057B0) of Chang Gung Memorial Hospital Keelung Branch.

From January 2, 2013, to December 21, 2015, consecutive patients who received colorectal surgery at Chang Gung Memorial Hospital Keelung Branch were identified on the basis of the International Classification of Diseases, Ninth Revision, disease codes (codes 153, 153.0-9, 154, 154.0-3, and 154.8) and procedure codes (codes 457.1-4, 457.5, 457.6, and 485). Readmission was defined as a hospital admission within 30 days after the index admission discharge. Only patients who received procedures performed by colorectal surgeons with a surgical indication of curative or palliative resection for malignant neoplasm were included in this study. Patients who had a concurrent

surgery on another organ or body cavity (e.g., combined hepatectomy or lung wedge resection), had a readmission within 30 days for adjuvant chemotherapy or staged operation, had a readmission within 30 days due to an irrelative reason (e.g., trauma), or died during the index admission were excluded (Fig. 1). A retrospective chart review was conducted using the patients' electronic medical charts, including inpatient and outpatient records.

Data collection

The patients' characteristics such as sex, age, body mass index (BMI), length of hospital stay (LOS), tobacco use (current only), alcohol use (current only), and betel nut use (current only) were collected. Information on perioperative medical condition was obtained by calculation of the Charlson comorbidity score³ and American Society of Anesthesiologist (ASA) score. Additional information on clinical status and perioperative conditions was collected, including history of coronary artery disease (CAD), cerebral vascular accident, end-stage renal disease (ESRD), hepatitis B or C virus infection, preoperative weight

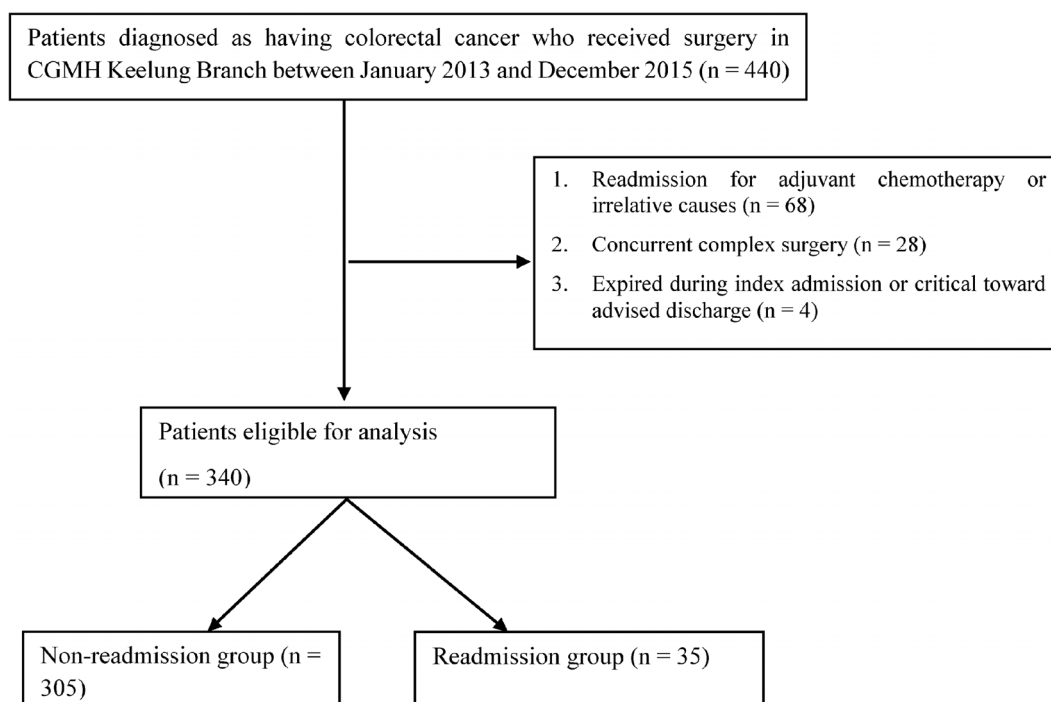


Fig. 1. Flowchart of the patient selection process.

loss, and chronic obstructive pulmonary disease.

Procedures were defined by the surgical removal of colorectal segments (right, left, transverse, anterior resection, total, and subtotal). Other procedures such as transrectal polypectomy, the Hartmann procedure, abdominal peritoneal resection, and stoma creation were also included for analysis.

During the index admission, the following major complications were found: generalized peritonitis, organ-specific surgical site infection, cerebrovascular accident or myocardial infarction during the perioperative period, septic shock, and unplanned reintubation. Minor complications were defined as superficial surgical site infection, stress ulcer, minor leakage without surgical intervention, paralytic ileus, urinary tract infection, and pneumonia.

Statistical analysis

Data analysis was performed using the SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA). Demographic factors were compared between the two groups by using the chi-square or Student *t* test. A two-tailed *p* value of < 0.05 was considered statistically significant. Significant predictors in the univariate analysis with *p* values of < 0.1 were included in the multivariate logistic regression analysis. Odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated using the Cox proportional-hazards model.

Results

From 2013 to 2015, 440 patients were diagnosed as having colorectal adenocarcinoma and received colorectal surgery either with curative or palliative intent. The exclusion criteria included concurrent complex surgery, readmission for adjuvant chemotherapy or scheduled staged operation, and death during index admission. A total of 340 patients were included in our study. Patient characteristics, procedures, and postoperative events were evaluated as risk factors of readmission (Table 1). The mean age was 68.23 ± 12.09 years (range, 37–96 years), and the median LOS was

10 days. Most of the patients were male ($n = 201$; 59.1%). The Charlson comorbidity score³ was determined as a measure of the preoperative medical condition of our patients.

Surgical resection included right hemicolectomy (27.1%), transverse colectomy (1.8%), left hemicolectomy (9.4%), high anterior resection (30.9%), low anterior resection (22.4%), combined abdominoperitoneal resection (2.9%), Hartmann procedure (1.2%), total colectomy (0.9%), subtotal colectomy (2.6%), and other procedures (1.8%). Among the patients who received surgical resection, 332 (97.6%) had an elective surgery. Minimal invasive surgery was performed in 35 patients (10.3%). A total of 192 patients (56.5%) had a tumor grading that indicated a localized disease.

Among the 340 patients who received colorectal surgery, 10.2% ($n = 35$) were readmitted within 30 days after discharge. The most common etiology was urinary tract infection (23%), followed by ileus (20%), superficial/deep surgical site infection (17%), stress ulcer-related gastrointestinal bleeding (17%), pneumonia (14%), nonspecific abdominal pain or diarrhea (6%), and deep organ space infection (3%) (Table 2).

The patients who were readmitted were more likely to have longer LOS, multiple comorbidities, hypoalbuminemia, and major postoperative complications during the index admission. In the univariate analysis, the Charlson comorbidity score (OR, 1.166; $p < 0.008$), LOS (OR = 1.032, $p = 0.028$), albumin (OR, 0.588; $p = 0.03$), old stroke history (OR, 2.948; $p = 0.032$), ASA (OR, 2.030; $p = 0.016$) and major postoperative complications (OR, 6.104; $p < 0.001$) were statistically significant. However, in multivariate model, only the postoperative major complications were statistically significant (OR, 4.126; $p = 0.012$; (Table 3).

The postoperative complications rate was 20.8% ($n = 71$). The major complication rate was 5.5% ($n = 19$), 9 cases (47.3%) were diagnosed as anastomosis leakage with associated intraabdominal abscess or peritonitis, of which 4 required additional surgical intervention (e.g., colostomy or ileostomy) during the index admission. The other patients were treated with total parenteral nutrition and intravenous antibiotic therapy. Five patients (26.3%) had deep organ space

Table 1. Demographic characteristics between non-readmission and readmission groups

Variables	Non-readmission (n = 305)	Readmission (n = 35)	Total (n = 340)	p value
Male (%)	183 (60.0)	18 (51.4)	201 (59.1)	0.329
Age (mean \pm SD)	67.96 \pm 11.81	70.54 \pm 14.27	68.23 \pm 12.09	0.309
CCS (mean \pm SD)	6.33 \pm 2.94	7.80 \pm 3.43	6.48 \pm 3.02	0.006
LOS (mean \pm SD)	15.49 \pm 9.34	19.51 \pm 13.49	15.91 \pm 9.90	0.094
BMI \geq 30 (%)	15 (5.7)	0	15 (5.1)	0.379
Albumin (mean \pm SD)	3.88 \pm 0.61	3.57 \pm 0.72	3.85 \pm 0.63	0.007
Comorbidities				
Diabetes mellitus (%)	78 (25.6)	14 (40.0)	92 (27.1)	0.069
Previous CVA (%)	20 (6.6)	6 (17.1)	26 (7.6)	0.038
End-stage renal disease (%)	13 (4.3)	4 (11.4)	17 (5.0)	0.085
CAD (%)	17 (5.6)	3 (8.6)	20 (5.9)	0.446
COPD (%)	10 (3.3)	3 (8.6)	13 (3.8)	0.139
HBV/HCV carrier (%)	35 (11.5)	2 (5.7)	37 (10.9)	0.400
Pre-op weight loss (%)	28 (9.2)	4 (11.4)	32 (9.4)	0.758
ASA (mean \pm SD)	2.62 \pm 0.62	2.89 \pm 0.58	2.64 \pm 0.62	0.014
Initial diagnosis				
A-colon cancer (%)	77 (25.2)	11 (31.4)	88 (25.9)	0.429
T-colon cancer (%)	25 (8.2)	2 (5.7)	27 (7.9)	> 0.999
D-colon cancer (%)	27 (8.9)	2 (5.7)	29 (8.5)	0.753
S-colon cancer (%)	83 (27.2)	12 (34.3)	95 (27.9)	0.377
Rectal cancer (%)	99 (32.5)	11 (31.4)	110 (32.4)	0.902
Elective operation (%)	298 (97.7)	34 (97.1)	332 (97.6)	0.585
Surgical procedure				
Right hemicolectomy (%)	83 (27.2)	9 (25.7)	92 (27.1)	0.850
Left hemicolectomy (%)	31 (10.2)	1 (2.9)	32 (9.4)	0.226
Transverse colectomy (%)	5 (1.6)	1 (2.9)	6 (1.8)	0.482
Stoma creation (%)	58 (19.0)	11 (31.4)	69 (20.3)	0.084
HAR (%)	92 (30.2)	13 (37.1)	105 (30.9)	0.397
LAR (%)	70 (23.0)	6 (17.1)	76 (22.4)	0.435
Hartmann (%)	3 (1.0)	1 (2.9)	4 (1.2)	0.354
Total colectomy (%)	2 (0.7)	1 (2.9)	3 (0.9)	0.279
Subtotal colectomy (%)	8 (2.6)	1 (2.9)	9 (2.6)	> 0.999
APR (%)	10 (3.3)	0	10 (2.9)	0.607
Other (%)	5 (1.6)	1 (2.9)	6 (1.8)	0.482
Minimal invasive surgery (%)	33 (10.8)	2 (5.7)	35 (10.3)	0.556
Pathology staging				
Localized, stage I-II (%)	177 (58.0)	15 (42.9)	192 (56.5)	0.086
Postoperative complications				
Major (%)	12 (3.9)	7 (20.0)	19 (5.5)	< 0.001
Minor (%)	44 (14.4)	8 (22.8)	52 (15.2)	0.189

LOS: length of stay; CCS: Charlson comorbidity score; BMI: body mass index.

Table 2. Main reasons of readmission

Reason for readmission	N (total = 35)	Proportion of patient readmitted (%)
Urinary tract infection	8	23
Ileus	7	20
Superficial or deep surgical site infection	6	17
GI bleeding	6	17
Pneumonia	5	14
Nonspecific abdominal pain, nausea, vomiting, or diarrhea	2	6
Deep organ space infection	1	3

Table 3. Univariate and multivariate analysis of risk factor in readmission

Predictor	Univariate			Multivariate		
	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
Carlson comorbidity index	1.166	1.042-1.306	0.008	1.053	0.888-1.248	0.552
Length of stay	1.032	1.003-1.061	0.028	1.003	0.968-1.039	0.882
Albumin	0.588	0.363-0.951	0.03	0.914	0.492-1.699	0.777
Diabetes mellitus	1.94	0.941-4.00	0.073	1.364	0.583-3.191	0.474
Old stroke history	2.948	1.097-7.927	0.032	1.873	0.616-5.696	0.268
ESRD	2.898	0.89-9.434	0.077	1.380	0.309-6.163	0.673
ASA	2.030	1.141-3.612	0.016	1.178	0.592-2.342	0.641
Stoma creation	1.952	0.905-4.211	0.088	1.583	0.683-3.667	0.284
Advanced stage	1.844	0.909-3.739	0.09	1.347	0.547-3.316	0.518
Major complications	6.104	2.224-16.752	< 0.001	4.126	1.369-12.442	0.012

infection that needed percutaneous drainage during the index admission. Two patients (10.5%) had an unplanned reintubation due to pneumonia with septic shock. One patient had a postoperative transient ischemic attack and seizure. Another patient had an acute myocardial infarction, and emergent percutaneous coronary angioplasty was arranged after the diagnosis. One patient had a hypovolemic shock due to stress ulcer-related bleeding that required transarterial embolization (Table 4).

Discussion

Thirty-day readmission rate has been used as a measure of surgical quality and a crucial indicator for surgeons to identify patients at risk of developing postoperative adverse events or readmission. However, owing to the limited study period and small number of patients included in our study, our results may not reflect the true impact of readmission on the quality of our health care.

In our study, the readmission rate was approxi-

mately 10%, similar to those reported in recent studies.^{4,5} However, in other studies, the primary outcome definition may be heterogeneous. Most studies observe readmission usually within 30 days after hospital discharge, but other studies extend this period up to 90 days.^{6,7}

In the univariate analysis, the CCS, LOS, albumin level, ASA score, postoperative complications, and previous stroke history were associated with readmission. However, in the multivariate analysis, because these covariates highly correlated with each other, only the occurrence of postoperative complication was associated with readmission ($p = 0.012$). The patients who had postoperative complications had 4 times higher odds of readmission than the patients who did not develop major adverse events. Similarly to a review study that used data from the Michigan Surgical Quality Collaborative database for elective colectomy-related readmission analysis, the postoperative complications highly correlated with readmission while the preoperative factors had less direct influence on readmission in our study.⁸

Postoperative complications such as anastomosis

Table 4. Major complications during index admission

	N (total = 19)	Ratio of major complications rate (%)
Anastomosis leakage with peritonitis or intraabdominal abscess	9	47.3
Deep organ space infection	5	26.3
Unplanned reintubation	2	10.5
Transient ischemic attack	1	5
Acute myocardial infarction	1	5
GI bleeding with hypovolemic shock	1	5

leakage after colorectal surgery had severe impacts on patient survival and quality of life in our study. Nine patients had an anastomosis leakage that needed repeated surgical intervention or long-term antibiotic treatment. The other major complication was deep organ-specific abscess formation that needed percutaneous drainage. These 2 types of major complications may be modified or decrease severity if patients' perioperative factors are accessed and corrected meticulously, including aggressive nutritional support, adequate prevention antibiotics, use of new techniques for bowel perfusion detection, and adequate index surgical drainage. With these efforts, the incidence of surgery-associated infection and readmission rate may be further reduced.

During the study period, the use of minimally invasive procedures was limited because of immature skill of surgeons and faculties. However, the increasing number of cases of minimally invasive surgery in our field (from 10% to 40% in the recent 2 years) had significant decreases in LOS, which may impact the post-discharge readmission rate.^{9,10} On the other hand, worldwide application of the "enhanced recovery after surgery" protocol had also improved patient postoperative recovery and reduced the number of unplanned readmissions.¹¹

This study was limited by the characteristics of a retrospective study, single-institute experience, relatively small sample size, and short study period. Nevertheless, the results implied that index surgery had a significant impact on the readmission of patients who received colorectal cancer surgery.

Conclusion

The predictive factor in our study was the postoperative complications of colorectal surgery, and preoperative patient factors had less impact on the readmission rates.

Although several important patient-related fac-

tors, such as age, albumin level, ASA class, and old stroke history were not found to be independent predictors of 30-day readmission. However, they must contribute to some degree by increasing the risk for complications. In our study, we suggest current strategies addressing readmission rates should focus on reducing preventable complications while still accepting that much may not be completely avoidable.

References

1. Damle RN, Alavi K. Risk factors for 30-d readmission after colorectal surgery: a systematic review. *J Surg Res* 2016; 200(1):200-7.
2. Bartlett EK, et al. Postdischarge occurrences after colorectal surgery happen early and are associated with dramatically increased rates of readmission. *Dis Colon Rectum* 2014;57(11): 1309-16.
3. Charlson ME, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40(5):373-83.
4. Greenblatt DY, et al. Readmission after colectomy for cancer predicts one-year mortality. *Ann Surg* 2010;251(4):659-69.
5. Al-Mazrou AM, et al. Characterization of readmission by day of rehospitalization after colorectal surgery. *Dis Colon Rectum* 2017;60(2):202-12.
6. Lucas DJ, Pawlik TM. Readmission after surgery. *Adv Surg* 2014;48:185-99.
7. Azimuddin K, et al. Readmissions after colorectal surgery cannot be predicted. *Dis Colon Rectum* 2001;44(7):942-6.
8. Therese G. Kerwel. Risk factors for readmission after elective colectomy: postoperative complications are more important than patient and operative factors. *Dis Colon Rectum* 2014; 57:98-104.
9. Li MZ, Meta-analysis of laparoscopic versus open colorectal surgery within fast-track perioperative care. *Dis Colon Rectum* 2012;55:821-7.
10. Biondi A, et al. Laparoscopic vs. open approach for colorectal cancer: evolution over time of minimal invasive surgery. *BMC Surg* 2013;13 Suppl 2:S12.
11. Zhuang CL, Ye XZ. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. *Dis Colon Rectum* 56:667-78.

原 著

大腸直腸癌術後 30 天內再住院率之原因分析

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目的 臨床上病患重返率常被視為醫療照護品質指標。非預期內的再住院可能會造成醫療資源上的負擔、病患預後及術後恢復品質的下降。這篇研究旨在分析造成大腸直腸癌術後出院的 30 日內再住院之原因。

方法 研究收錄了從 2013 年 1 月至 2015 年 12 月共 440 位初診斷為大腸直腸癌並接受根治性或姑息性手術切除的病患，首次住院期間合併其他術式如肝切除或膀胱切除、30 日內再住院化療病患等則排除不收案。此篇研究採用回顧性病歷收集病患資料、術式及造成再住院之原因。 χ^2 test 使用於比較類別變數、Student t test 則用於連續變數。顯著意義之變因再使用單變量及多變量分析來找出造成再住院之原因。

結果 在比較收案條件後，共 340 位病患符合條件。其中 35 位為接受大腸直腸癌術後出院 30 日內再住院之病患。於單變量分析中，多重合併症、較高的 ASA 分數、低白蛋白指數、中風病史及首次住院術後發生重大併發症為危險因子；然而，在多變量分析中，造成收案族群 30 日內再住院之唯一獨立危險因子為首次住院有無發生術後重大合併症。

結論 雖然病患本身相關因子並未對再住院率有直接顯著影響，但可以從這篇研究中瞭解到術後發生併發症為獨立危險因子，因此可讓我們來重新擬定預防 30 日內再住院率的策略。

關鍵詞 30 日再住院率、大腸直腸手術、術前及術後因子。

Original Article

Comparison of the Effect of Preoperative Colonoscopy and Barium Enema on the Prognosis of Colon Cancer Patients

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Key Words

Colonoscopy;
Barium enema;
Colon cancer

Purpose. Complete colonoscopy is usually performed preoperatively in colon cancer patients to exclude synchronous colonic tumors. Some surgeons avoid preoperative endoscopy in cases of a colon tumor with a narrow bowel lumen to avoid dissemination of the tumor cells during the colonoscopy procedure with squeeze pressure. The purpose of this study was to determine whether double-contrast barium enema is an alternative to preoperative whole-colon screening in colon cancer patients with respect to oncologic outcomes.

Methods. We retrospectively reviewed the medical records of patients diagnosed with colon adenocarcinoma and underwent surgery at the Tri-Service General Hospital, Taipei, Taiwan, between January 2008 and December 2013. The patients were randomly divided into two groups. One group underwent complete colonoscopy and the other a double-contrast barium enema for preoperative whole-colon screening. The outcome variables analyzed were postoperative recurrence, disease-free survival, and overall survival.

Results. Three-hundred and two patients were enrolled in this study. They were divided into two groups: 152 (50.3%) who underwent complete colonoscopy and 150 (49.7%) who underwent double-contrast barium enema for newly diagnosed colon cancer. There were no statistically significant differences in pathologic staging between the two groups. Furthermore, recurrence rate, disease-free survival, and overall survival also showed no differences.

Conclusions. In colon cancer patients undergoing preoperative whole-colon screening, double-contrast barium enema is an alternative option when preoperative colonoscopy is not under consideration due to narrowing of the bowel lumen. However, these two screening tools had no effect on the oncologic outcomes of colon cancer patients.

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Colorectal cancer (CRC) is the third leading cause of cancer-related death in Taiwan.¹ Multiple techniques have been used for colorectal cancer screening, including the fecal occult blood test (FOBT), fe-

cal immunochemical testing, colonoscopy, double-contrast barium enema (DCBE), and computed tomography (CT) colonography.²⁻⁴

Colonoscopy is a well-established procedure for

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the evaluation of lower gastrointestinal tract diseases, including colorectal polyps and cancer, and has become one of the most popular choices for CRC screening because of the possibility of simultaneous diagnosis and treatment.⁵ Complete colonoscopy is usually attempted preoperatively to rule out synchronous malignant colorectal cancers, which occur in 5%-10% of patients.⁶

However, some surgeons fear that preoperative whole-colon screening via colonoscopy with squeeze pressure might cause dissemination of tumor cells in cases of colon tumors with a narrow bowel lumen. Others fear the possibility of distant tumor cell implantation after colonoscopy with tumor biopsy.

The purpose of this study was to determine whether double-contrast enema is an alternative to preoperative whole-colon screening of colon cancer patients with a narrow bowel lumen with regard to oncologic outcomes.

Materials and Methods

We retrospectively reviewed the medical records of patients who were diagnosed with colon adenocarcinomas and underwent surgery at the Tri-Service General Hospital, Taipei, Taiwan, between January 2008 and December 2013. Patients with obstructed right-side colon cancer, distant metastasis, synchronous colorectal cancer or other malignancies were excluded from the study. The diagnosis of colon cancer with bowel lumen narrowing was confirmed by colonoscopy and pathological analysis, according to the American Joint Committee on Cancer (AJCC) 8th edition. The patients were randomly divided into two groups. One group underwent complete colonoscopy and the other group, double-contrast barium enema for preoperative whole-colon screening. Incomplete colonoscopy was defined as any colonoscopy that did not reach the cecum. T and N staging was performed based on the pathology of the surgical specimen, and all surgical specimens were dissected by a fixed team of gastrointestinal pathologists within the hospital. CT was used to evaluate distant metastasis in all patients. Follow-up was conducted at three-month inter-

vals over a period of two years and at six-month intervals for the succeeding three years. Follow-up indicators included FOBT, abdominal ultrasonography, chest radiography, serum tumor marker [carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9)] level assessment, colonoscopy, and CT scanning of the abdomen and pelvis. Patients underwent colonoscopy three months after surgery and annually thereafter. Biopsies were performed for all cases of suspicious recurrence. Metachronous cancer was defined as a secondary colon cancer occurring more than 6 months after the index cancer.

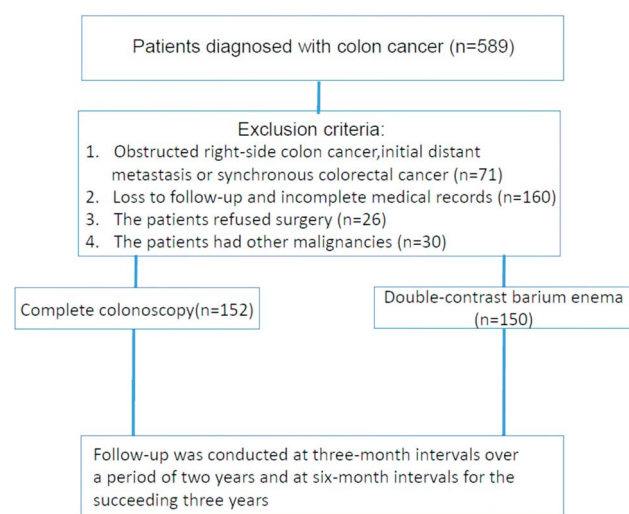
Clinical data, including age, sex, clinical stage, pathological stage, and overall recurrence, were analyzed. All statistical analyses were completed using SPSS software for Windows (IBM, New York, USA), and a significance level of 5% was used for all analyses.

Results

The characteristics of all patients are shown in Table 1. A total of 589 patients diagnosed with colon adenocarcinoma and admitted to Tri-Service General Hospital, Taipei, Taiwan between January 2008 and December 2013 were recruited for this study. We excluded 71 patients who were diagnosed with obstructed right-side colon cancer, initial distant metastasis or synchronous colorectal cancer; 160 patients were lost to follow-up after their operation or had incomplete medical records; 26 patients refused surgical treatment because of advanced age or existing comorbidities; and 30 patients had other malignancies. The remaining 302 patients with newly diagnosed colon cancer with bowel lumen narrowing were enrolled in this study and analyzed (Fig. 1). The 302 patients were divided into two groups: 152 (50.3%) underwent complete colonoscopy and 150 (49.7%) underwent double-contrast barium enema to rule out synchronous colon tumors. The average age of the patients was 68.9 years in the complete colonoscopy group and 67.9 years in the double-contrast barium enema group. There were no statistically significant differences in the pathologic stage or overall recurrence for

Table 1. Patient characteristics and comparison of patients who underwent complete colonoscopy and barium enema

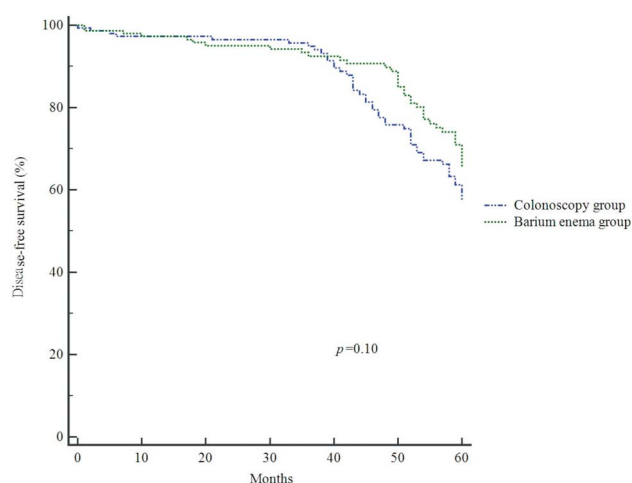
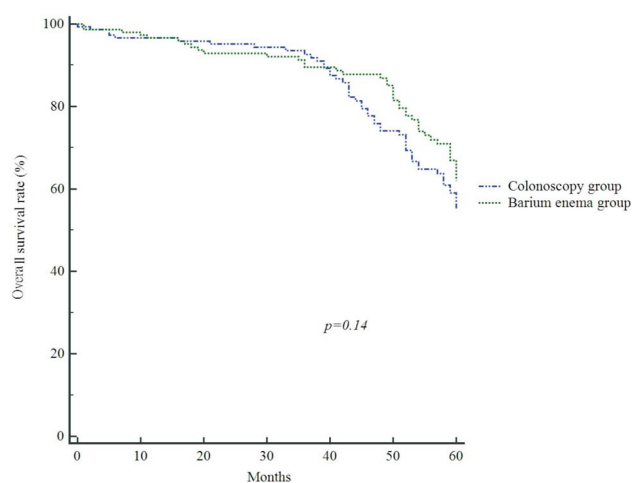
	Complete colonoscopy (n = 152)	Barium enema (n = 150)	p-value
Age (Mean \pm SD)	68.3 \pm 13.0	67.9 \pm 12.9	0.82
Sex			0.27
Male	74	82	
Female	78	68	
Tumor location			0.88
Transverse	30	27	
Descending	45	40	
Sigmoid	77	83	
Pre-op clinical stage			0.25
I	23	19	
II	57	61	
III	72	70	
Pathological stage			0.12
I	33	16	
II	67	72	
III	52	62	
T staging			0.23
T1	17	10	
T2	20	14	
T3	105	119	
T4	10	7	
N staging			0.15
N0	100	88	
N1	29	38	
Recurrence	15 (8.7%)	16 (10.7%)	0.58
Survival	57 (33.1%)	61 (40.7%)	0.17

**Fig. 1.** Flowchart showing the management of patients diagnosed with colon cancer.

patients in the complete colonoscopy group and double-contrast barium enema group. In addition, disease-free survival (Fig. 2) and overall survival (Fig. 3) were not significantly different between the groups.

Discussion

Synchronous colorectal cancers have been reported in 5%-10% of patients, and synchronous adenomatous polyps in colon cancer have been reported in 15%-50% of cases.^{7,8} Therefore, complete colonoscopy is usually attempted preoperatively in all colorectal cancer patients to rule out the presence of synchronous malignant colorectal lesions, as the presence

**Fig. 2.** Disease-free survival.**Fig. 3.** Overall survival.

of synchronous lesions often alters the surgical plan. In the presence of colon cancer, many colonoscopists prefer not to perform complete colonoscopy to avoid the risk of tumor cell implantation into the damaged site of colonic mucosa.⁹ Besides, tumor cell dissemination may occur during colonoscopic procedures because of mechanical alteration of the colon through insufflation of air, advancement of the colonoscope, and application of transabdominal pressure.¹⁰

In one study, blood samples were examined using a cytokeratin (CK) 20 reverse-transcriptase polymerase chain reaction (RT-PCR)-based protocol to determine the rate of tumor cell dissemination into peripheral circulation before and after colonoscopic stent insertion for colorectal cancer. Increasing levels of CEA and CK 20 mRNA expression were noted in the peripheral circulation of patients with colorectal cancer.¹¹ These results indicate the possibility of hematogenous tumor cell dissemination during colonoscopy. However, the presence of circulating tumor cells in the peripheral circulation does not necessarily result in the metachronous recurrence of colon cancer, as the implantation of circulating tumor cells appears to be highly inefficient, and most of the tumor cells are rapidly destroyed.¹² Maeda et al. performed in vivo studies that suggested exfoliated cells maintain their viability and ability to implant only when they travel a short distance through the colon,¹³ and the majority of exfoliated colorectal cancer cells were found within 5 cm above or below the tumor. In addition, the intrinsic characteristics of the colonic mucosa also restrict tumor cell implantation, and the distribution of exfoliated cancer cells may also explain the low incidence of mucosal implantation after colonoscopic procedures.¹⁴

Sometimes, it is difficult to complete a colonoscopy because of tumor obstruction due to a narrow bowel lumen, patient discomfort, inadequate bowel preparation, and fixation or adhesions from prior surgery. It has been reported that preoperative colonoscopy is not possible in as many as 50% of patients.¹⁵ The consequence of an unsuccessful preoperative procedure is the requirement for a repeat examination immediately after the operation. Barlow et al.¹⁶ suggested performing a colonoscopy after surgery when the colonoscopy is more likely to be successful. Intra-

operative colonoscopy is another option when preoperative complete colonoscopy is not possible. However, not all researchers agree on the effectiveness of intraoperative colonoscopies due to the increased surgical time and possible risk of infection.¹⁷

There are little data on the recommendations made for preoperative whole-colon screening of colon cancer patients with incomplete colonoscopy. In our study, we performed double-contrast barium enemas in some of the patients with incomplete preoperative colonoscopy, and the 5-year overall survival, 5-year disease-free survival, and postoperative recurrence rates were not statistically different from the preoperative colonoscopy group. A review article suggested that patients with incomplete colonoscopy should undergo a second colonoscopy rather than DCBE given the inadequate sensitivity and accuracy of DCBE and the suboptimal and noninterpretable nature of DCBE in some patients.¹⁸ However, our study yielded data supporting the use of DCBE as a preoperative whole-colon screening tool, without an effect on oncologic outcomes, in colon cancer patients.

Conclusions

Patients who are newly diagnosed with colon cancer should undergo preoperative whole-colon screening, as the presence of synchronous lesions often alters the treatment plan. Double-contrast barium enema is an alternative option when preoperative colonoscopy is not applicable in cases of colon tumors because of narrowing of the bowel lumen. Both colonoscopy and double-contrast barium enema have no effect on the oncologic outcomes of colon cancer patients.

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References

1. Wang YW, Chen HH, Wu MS, Chiu HM, Taiwanese Nation-

- wide Colorectal Cancer Screening Program. Current status and future challenge of population-based organized colorectal cancer screening: lesson from the first decade of Taiwanese program. *J Formos Med Assoc* 2018;117(5):358-64.
2. Durdey P, Weston PM, Williams NS. Colonoscopy or barium enema as initial investigation of colonic disease. *Lancet* 1987;2(8558):549-51.
 3. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA Cancer J Clin* 2008;58(3):130-60.
 4. Kewenter J, Brevinge H, Engaras B, Haglind E. The yield of flexible sigmoidoscopy and double-contrast barium enema in the diagnosis of neoplasms in the large bowel in patients with a positive Hemoccult test. *Endoscopy* 1995;27(2):159-63.
 5. Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale-update based on new evidence. *Gastroenterology* 2003;124(2):544-60.
 6. Sollenberger L, Eisenstat T, Rubin R, Salvati E. Is preoperative colonoscopy necessary in carcinoma of the colon and rectum? *Am Surg* 1988;54(2):113-5.
 7. Burns FJ. Synchronous and metachronous malignancies of the colon and rectum. *Dis Colon Rectum* 1980;23(8):578-9.
 8. Langevin JM, Nivatvongs S. The true incidence of synchronous cancer of the large bowel. A prospective study. *Am J Surg* 1984;147(3):330-3.
 9. Basha G, Ectors N, Penninckx F, Filez L, Geboes K. Tumor cell implantation after colonoscopy with biopsies in a patient with rectal cancer: report of a case. *Dis Colon Rectum* 1997;40(12):1508-10.
 10. Koch M, Kienle P, Sauer P, et al. Hematogenous tumor cell dissemination during colonoscopy for colorectal cancer. *Surg Endosc* 2004;18(4):587-91.
 11. Maruthachalam K, Lash G, Shenton B, Horgan A. Tumour cell dissemination following endoscopic stent insertion. *Br J Surg* 2007;94(9):1151-4.
 12. Weiss L. Metastatic inefficiency. *Adv Cancer Res* 1990;54:159-211.
 13. Maeda K, Hanai T, Sato H, et al. Intraluminal exfoliated cancer cells and effectiveness of bowel ligatures during sigmoidectomy for sigmoid colon cancer. *Surg Today* 2014;44(2):297-301.
 14. Tan WJ, Ng NZ, Chen YD, et al. Synchronous polypectomy during endoscopic diagnosis of colorectal cancer - is the risk of tumour implantation at the polypectomy site significant? *BMC Gastroenterol* 2018;18(1):133.
 15. Tate JJ, Rawlinson J, Royle GT, Brunton FJ, Taylor I. Pre-operative or postoperative colonic examination for synchronous lesions in colorectal cancer. *Br J Surg* 1988;75(10):1016-8.
 16. Barlow AP, Thompson MH. Colonoscopic follow-up after resection for colorectal cancer: a selective policy. *Br J Surg* 1993;80(6):781-4.
 17. Torralba JA, Robles R, Parrilla P, et al. Subtotal colectomy vs. intraoperative colonic irrigation in the management of obstructed left colon carcinoma. *Dis Colon Rectum* 1998;41(1):18-22.
 18. Kao KT, Tam M, Sekhon H, Wijeratne R, Haigh PI, Abbas MA. Should barium enema be the next step following an incomplete colonoscopy? *Int J Colorectal Dis* 2010;25(11):1353-7.

原 著

大腸鏡檢查與鋇劑攝影對大腸癌患者 預後影響的比較

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目的 大腸癌病人手術前常接受大腸鏡檢查以排除其他部位同時之大腸癌病灶。一些外科醫師避免因腫瘤造成腸腔狹窄的情況去完成全大腸鏡檢查，以避免因擠壓導致腫瘤細胞的播種。這個研究的目的是探討鋇劑攝影是否能夠成為大腸鏡檢以外另一種可選擇的術前篩檢工具。

方法 經由回溯性病歷分析 2008 年 1 月至 2013 年 12 月被診斷為大腸癌並接受手術的患者的病歷。一組患者進行了完整的大腸鏡檢查，另一組患者則進行了鋇劑攝影。分析兩組病人在術後復發率，無病生存率和總體存活率是否存在差異。

結果 共有 302 名患者被收入了這項研究。他們被分為兩組：152 名患者 (50.3%) 接受了完全結腸鏡檢查，150 名患者 (49.7%) 接受了鋇劑攝影。兩組比較下，病理分期及復發率無統計學差異。此外，無病存活率和總體存活率也沒有顯著差異。

結論 因腸腔狹窄而未完成術前大腸鏡檢查時，鋇劑攝影是另一種選擇。然而，這兩種篩檢工具對結腸癌患者的預後沒有影響。

關鍵詞 大腸鏡、鋇劑攝影、大腸癌。

Original Article

Risk Factor Analysis on Distant Metastasis and Local Recurrence after Curative Resection in Early-stage Middle and Low Rectal Cancer

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Key Words

Early-stage rectal cancer;

Distant metastasis;

Local recurrence;

Risk factor analysis

Purpose. The disease recurrence after curative surgery on early stage rectal cancer is frustrated and the patient number is scarce. This study aims to find out the risk factors in distant metastasis and local recurrence separately.

Methods. Patients who were diagnosed with pT1 or pT2 rectal adenocarcinoma and treated by local excision or radical resection between January 2005 and December 2016 were retrospectively recruited in this study. The risk factors for recurrence were identified by p value < 0.1 in Log-rank test from Kaplan-Meier survival analysis. Cox proportional hazard model was adopted individually to the risk factors for distant and local recurrences.

Results. There were 350 patients enrolled in this study. The length of follow up time was 73.8 [46.1-107.6] (months). “Pre-operative CEA ≥ 5 (ng/mL)” [hazard ratio = 4.02 (1.42-11.36)] ($p = 0.009$) and “Early post-operative morbidity” [hazard ratio = 3.22 (1.17-8.83)] ($p = 0.023$) were risk factors for distant metastasis; “Resection margin ≤ 0.1 (cm)” [hazard ratio = 6.12 (1.48-25.46)] ($p = 0.013$) was risk factors for local recurrence. “Lympho-vascular invasion” [hazard ratio = 2.51 (0.87-7.26)] and “Tumor Diameter ≥ 3 (cm)” [hazard ratio = 5.08 (0.90-28.57)] had borderline significance ($p < 0.1$).

Conclusions. For early-stage rectal cancer, recurrence rate is low after curative surgery. We suggest carefully follow-up plan for those who has high-risk factors. Further study on follow-up strategy and adjuvant treatment are needed to achieve better survival.

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Cancer remains top 1 of the most common 10 causes of death about 4 decades. In Taiwan, colorectal cancer has 1st incidence rate of all malignant disease, 3rd mortality rate in male and 4th mortality rate in female. As the implementation of occult blood test of stool for people above 50 years old, we screen out

more and more early-stage colorectal cancer by diagnostic colonoscopy. For those resectable cancers, even advanced stage, en-bloc surgical resection remains the first priority of various treatment options.¹ However, bowel resection may bring peri-operative morbidity, or impact of long-term quality of life, especially for

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those patients with middle and low rectal cancer.

In the past, the treatment guidelines for rectal cancer suggested radical resection, which including various approaches. However, those treatment sometimes accompanied with long-term lifestyle modifications.²⁻⁴ LAR syndrome, for example, is one of well-known term for those suffers from fragmented stool, defecatory urgency, frequent bowel movement, or stool incontinence the worst.⁵ By the evolution of treatment on rectal cancer, anus-sparing surgery draws more and more attention. In the past, transanal excision, polypectomy, and transanal endoscopic microsurgery were reserved for pT1 tumor with low risk pathological factors. Precise pathological N stage is critical for colorectal cancer, as the adjuvant therapy is effective for those have high disease recurrent risk. Moreover, local excision with adjuvant chemoradiation brings less impact on anorectal function in comparison with radical resection.⁶ Therefore, more and more studies focused on local excision combined with or without neoadjuvant or adjuvant chemoradiation.

To date, aggressive tumor biology and therefore poor prognosis were considered to present short disease-free interval to occurrence of distant metastases.^{7,8} However, metastatic colorectal cancer still has low rates of complete cure and remains a therapeutic challenge.⁹ Consequently, patients with early distant metastasis after primary tumor resection have less chance to receive intensive but potentially curative multimodality treatment because they might be considered to poor prognosis.¹⁰

Rectal cancer seems to have different metastasis mechanism to colon cancer. The most common site of distant metastasis for colon cancer is liver; isolated metastasis at lung and local recurrence were reported to be the most recurrence site for rectal cancer from the statistics of National Cancer Institute's Surveillance of America.¹¹ There were some studies focused on the risk factors of tumor recurrence. The number of lymph nodes, vascular invasion and perineural invasion (PNI), and low microsatellite instability have been shown to be important predictors of distant metastasis in a classic study.¹² A study reported that lymphatic invasion was a high-risk factor for disease recurrence and worse disease-free survival (DFS) in

433 patients with colon cancer and 86 patients with rectal cancer. T2 tumors were at risk with borderline significance ($p = 0.065$).¹³

Due to scarce patient number, there was no study focusing only on rectal cancer published before. The purpose of this study is separately to find out the risk factors for local or distant metastasis of early stage rectal cancer.

Materials and Methods

Detailed data of 990 patients who were diagnosed with pT1 or pT2 rectal adenocarcinoma and treated by curative surgery between January 2005 and December 2016 were retrospectively recruited from the Colorectal Section Tumor Registry at the Chang Gung Memorial Hospital. This study was approved by the Institutional Review Board. Clinical staging was determined using computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET). Patients were excluded from this study for the following reasons: having synchronous colon cancer ($n = 116$); having rectal cancer 8 cm above anal verge ($n = 381$); receiving neoadjuvant CCRT ($n = 132$) for rectal cancer; with clinical evidence of distant metastases ($n = 3$); pathology data loss or proved to be melanoma, NET (neuroendocrine tumor), or GIST (gastrointestinal stromal tumor) ($n = 8$) (Fig. 1).

The available medical records included data on age, sex, body mass index (BMI), family cancer history, tumor location (centimeter away from the anal verge), maximal tumor diameter, preoperative carcinoembryonic antigen (CEA), albumin level, and hemoglobin level. All preoperative laboratory parameters were measured within 24 hours after admission. Tumor location was confirmed from anal verge with rigid sigmoidoscopy. Operation types were recorded as trans-abdominal resections or local excision. Pathological reports including tumor diameter (cm), resection margin (cm), pT and pN stage, tumor differentiation, lympho-vascular invasion (LVI), and perineural invasion (PNI) were examined. Operative records included operation method and the creation of a temporary or permanent ostomy. Adjuvant therapy included

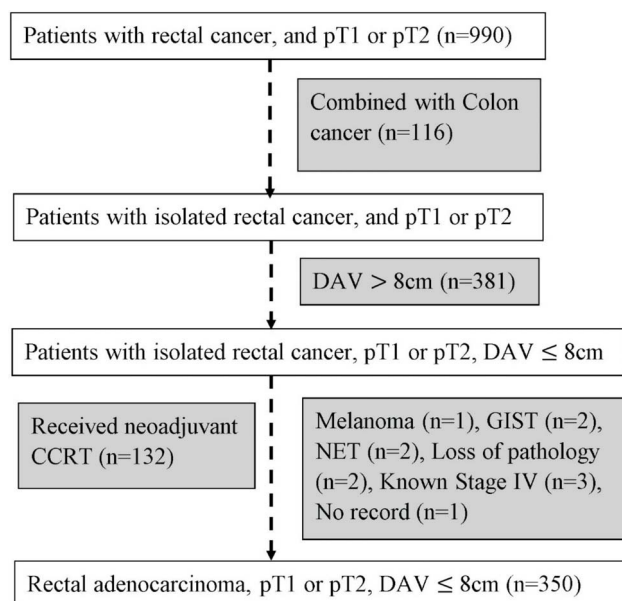


Fig. 1. Patient selection: 2005-2016. DAV: distance from anal verge; CCRT: concurrent chemoradiation; GIST: gastro-intestinal stromal tumor; NET: neuro-endocrine tumor.

chemotherapy or CCRT. Several chemotherapy regimens were adopted, including oral form combining tegafur and uracil, intravenous form fluorouracil and leucovorin (5-Fu/LV), and oxaliplatin plus intravenous 5-Fu/LV (FOLFOX). Adjuvant radiotherapy with long-course radiotherapy (5040 cGy delivered in 28 fractions) was implemented.

Postoperative complications were classified as early morbidity and late morbidity. Early morbidity was defined as postoperative complications occurring within 30 days, including wound-related (wound infection or wound dehiscence), pulmonary (atelectasis or pneumonia), cardiovascular (myocardial infarction, stroke or embolism), urinary (urinary tract infection or neurogenic bladder), gastrointestinal (obstruction, ileum or bleeding), and anastomosis-related (leakage, stenosis) complications. The late morbidity was defined as complications occurring after discharge and any event of readmission. Postoperative mortality was defined as death occurring within 30 days after operation.

Different physicians in the same department of this institute adopted similar follow-up routines. At the discretion of an individual physician, all patients were subjected to a follow-up program that included

outpatient visits every 3 months in the first 1 year and 6 months in the second with physical examinations, including digital rectal exams, and CEA tests. Scheduled CT or MRI scans every 6 months in the first 2 years, and colonoscopies annually in the first 2 years. Recurrent disease was confirmed by histology of colonoscopy biopsy specimens, re-operation, or radiological studies.

All statistical analyses were performed with IBM SPSS version 24.0 in this study. The risk factors for distant metastasis or local recurrence were identified by p value < 0.1 in Log-rank test from Kaplan-Meier survival analysis. Cox proportional hazard model was adopted individually to distant metastases and local recurrences. The results were reported as hazard ratios (HR) with a 95% CI. Two-sided p values with $p < 0.05$ showed statistical significance in the results.

Results

Between 2005 and 2016, 350 patients were identified. The age was 63.6 ± 12.6 (mean \pm SD, standard deviation), and the BMI was 24.3 ± 3.5 . There were 189 (54.0%) males and 133 (38.0%) cases with family cancer history. Pre-operative CEA was 1.9 [1.1-2.9] (ng/mL) (median [25 percentile-75 percentile]). Tumor location was marked as distance from anal verge (DAV): 6 [5-8] (cm) (Table 1). In the peri-operative days, 153 (43.7%) patients received temporary ileostomy or colostomy, and 28 (8%) patients had permanent stoma. The patients received one of two operation types: (1) 292 trans-abdominal resections (including 266 low anterior resections with staple anastomosis, 2 subtotal colectomy with staple anastomosis, 21 abdomino-perineal resections, and 3 Hartmann's procedures) by laparotomy or laparoscopy. (2) 58 Local excision (including trans-anal excision or polypectomy, and trans-anal endoscopic microsurgery). There were 76 (21.7%) patients had post-operative morbidity, which included 53 (15.1%) patients had early morbidity in post-operative 30 days, 35 (10.0%) patients had late morbidity after post-operative 30 days (Table 2).

The length of follow up time was 73.8 [46.1-107.6]

(months). 153 (43.7%) patients had temporary colostomy or ileostomy, and 28 (8.0%) patients had permanent colostomy or ileostomy. 83 (23.7%) patients received adjuvant therapy, including 57 (16.3%) of them received chemotherapy, and 26 (7.5%) received CCRT (Table 2).

There were 158 (45.1%) patients had T1 stage, while others were T2 stage. N stage was examined in 292 patients with trans-abdominal resection, and there were 62 (21.2%) patients had N+ stage (including 53 N1, and 9 N2). 47 (13.4%) patients had lympho-vascular invasion (LVI), while 21 (6%) patients had perineural invasion (PNI). There were 261 (74.6%) mod-

erate-differentiated, 80 (22.9%) well-differentiated, and 9 (2.6) poor-differentiated cancers. The tumor diameter was 2.7 [2.0-3.9] (cm), and the resection margin was 1.2 [0.5-2.0] (cm) (Table 3).

In the analysis on distant metastasis, “Pre-operative CEA ≥ 5 (ng/mL)” had hazard ratio (HR) = 4.02 (1.42-11.36) ($p = 0.009$), “Early post-operative morbidity” had HR = 3.22 (1.17-8.83) ($p = 0.023$), and “LVI” had HR = 2.51 (0.87-7.26) with borderline significance ($p = 0.090$) (Table 4). In the analysis on local recurrence, “Resection margin ≤ 0.1 (cm)” had HR = 6.12 (1.48-25.46) ($p = 0.013$), and “Tumor diameter ≥ 3 (cm)” had HR = 5.08 (0.90-28.57) with borderline significance ($p = 0.065$) (Table 5).

Table 1. Patient characteristics

Variable	All 350 patients (% or [Q1 - Q3])
Age	63.6 \pm 12.6*
BMI (kg/m ²)	24.3 \pm 3.5*
Male gender	189 (54.0)
Family cancer history	133 (38.0)
Pre-operative CEA (ng/mL)	1.9 [1.1-2.9]**
Pre-operative CEA ≥ 5	39 (11.1)
DAV (cm)	6 [5-8]**
DAV < 5	86 (24.6)

BMI: body mass index; CEA: carcinoembryonic antigen; DAV: distance from anal verge.

* Mean \pm SD (standard deviation). ** Median [25 percentile-75 percentile].

Table 2. Treatment and follow-up characteristics

Variable	All 350 patients (% or [Q1-Q3])
Operation type	
Trans-abdominal resection	292 (83.4)
Local excision	58 (16.6)
Post-op morbidity	76 (21.7)
Early	53 (15.1)
Late	35 (10.0)
Ostomy	
Temporary	153 (43.7)
Permanent	28 (8.0)
Adjuvant therapy	83 (23.7)
Chemotherapy	57 (16.3)
CCRT	26 (7.5)
Follow up length (month)	73.8 [46.1-107.6]*
Distant metastasis	18 (5.1)
Local recurrence	8 (2.3)

CCRT: concurrent chemoradiation.

* Median [25 percentile-75 percentile].

Discussions

In this retrospective study to 350 patients receive-

Table 3. Pathological characteristics

Variable	All 350 patients (% or [Q1-Q3])
Resection margin (cm)	1.2 [0.5-2.0]*
Tumor diameter (cm)	2.7 [2.0-3.9]*
T stage	
T1	158 (45.1)
T2	192 (54.9)
LVI	47 (13.4)
PNI	21 (6)
Differentiation	
Poor	9 (2.6)
Moderate	261 (74.6)
Well	80 (22.9)
N stage +	62 (21.2)**

LVI: lymphovascular invasion; PNI: peri-neural invasion.

* Median [25 percentile-75 percentile]. ** From 292 patients received trans-abdominal resection.

Table 4. Hazard ratio for distant metastasis

Variable	Hazard ratio (95% CI for Exp(B))	p value
Pre-operative CEA ≥ 5 (ng/mL)	4.02 (1.42-11.36)	0.009*
Early post-operative morbidity	3.22 (1.17-8.83)	0.023*
LVI	2.51 (0.87-7.26)	0.090
Tumor Diameter ≥ 3 (cm)	2.34 (0.80-6.85)	0.120
Resection margin ≤ 0.1 (cm)	1.98 (0.62-6.30)	0.248

CEA: carcinoembryonic antigen; LVI: lympho-vascular invasion.

* p value < 0.05 .

Table 5. Hazard ratio for local recurrence

Variable	Hazard ratio (95% CI for Exp(B))	<i>p</i> value
Resection margin ≤ 0.1 (cm)	6.12 (1.48-25.46)	0.013*
Tumor diameter ≥ 3 (cm)	5.08 (0.90-28.57)	0.065
DAV < 5 (cm)	3.42 (0.79-14.76)	0.099

DAV: distance from anal verge.

* *p* value < 0.05 .

ing curative surgery for early stage rectal cancer, we found “Pre-operative CEA ≥ 5 (ng/mL)” and “Early post-operative morbidity” as high-risk factor for distant metastasis. In the separate analysis, we found “Resection margin ≤ 0.1 (cm)” as a high-risk factor for local recurrence.

Pre-operative CEA

There were some studies found that pre-operative or pre-chemotherapy CEA elevation is related to disease recurrence or disease-free survival.¹⁴⁻¹⁹ However, there were some studies reported non-significant results of CEA elevation for disease recurrence and/or disease-free survival.²⁰ Besides, shorter time to recurrence was reported in patients with stage I colon cancer in a retrospective study.²¹

Post-operative morbidity

Our study showed 53 (15.1%) patients had early morbidity in post-operative 30 days. Eighteen of the 53 patients were favored with anastomotic leakage from both image study and clinical observation. A systematic review containing 14 studies and 11,353 patients, anastomotic leakage was associated with higher local recurrence rate but not distant metastasis rate.²² In our study, four of the 18 patients with anastomotic leakage had recurrence (3 distant metastases and 1 local recurrence).

Resection margin

In our study, we set distal margin from the tumor to the cutting edge of the specimen as “Resection margin”. Among 97 patients with distal margin of ≤ 1

mm, higher 5-year local recurrence rate (24.1% vs. 12.0%, $p = 0.005$) and worse 5-year disease-free survival (45.5% vs. 69.5%, $p < 0.001$) were noted from a retrospective study including 6,574 patients underwent anterior resection for rectal cancer.²³ For oncologic safety, resection margin should be ≥ 1 cm. Nevertheless, there were various definitions of “Positive resection margin” from previous studies, with 0.1 cm to 2 cm in low anterior resection. With the reference, we set microscopic resection margin ≤ 0.1 cm to analysis.

Local excision vs. radical resection

Local excision is suitable for cT1 with low pathological risk factors.^{24,25} There were some studies focused on local excision for T2 tumors, for example, a National Cancer Database Analysis in review of 4822 patients concluded that local excision with CCRT was not associated with worse overall survival in comparison to radical resection.²⁶ Another study use the same database concluded similar results in the comparison of 1,761 patients underwent transabdominal resection and 3,531 patients underwent local transanal excision with and without neoadjuvant chemoradiation.²⁷ A systematic review reported that local excision with adjuvant therapy for pT1 rectal tumors with high-risk pathologic factors can achieve acceptable long-term outcomes.²⁸ Another study also showed 5-year survival outcome from 53 patients with T1 lesions who treated with local excision and full-dose chemoradiotherapy.²⁹ A single-center experience for TEM with adjuvant therapy for early rectal cancer showed 98.6% disease-specific survival rate in 54 pT1 and 22 pT2 patients.³⁰ Though more and more patients were selected for local excision, higher local recurrence rate was reported in some studies.³¹⁻³⁴

Nevertheless, by the evolution of adjuvant treatment, local excision with adjuvant treatment is gradually accepted by colorectal surgeons. In our survival analysis with Kaplan-Meier method, local excision had similar local recurrence rate ($p = 0.645$), distant metastasis rate ($p = 0.917$) and disease-free survival rate ($p = 0.740$ in Log Rank test) to radical resection. Therefore, our study did not exclude patients receiv-

ing local excision with or without adjuvant chemotherapy.

Concern of N stage

Local excision does not provide accurate regional lymphatic stage (N stage in TMN), which potentially indicates tumor spreading, so there are some studies trying to find out risk factors of regional lymph nodes metastasis.³⁵⁻³⁸ Our study found out 62 patients with N stage positive from 292 radical resections. According to current guideline, N stage positive is a high-risk factor for disease-free survival, and adjuvant chemotherapy would be suggested to most of them. In our retrospective study, 7 of 62 patients with N stage positive did not receive adjuvant chemotherapy. Three of them died at post-operative 1st, 4th, and 7th year due to non-cancer related disease; four of them were still cancer-free for 1 to 7 years, but finally they were found with 4 distant metastases and 1 local recurrence. Old age and comorbidity were the reasons why they did not receive adjuvant therapy. We found that N stage positive was not significant to neither distant nor local recurrence, and this finding might be resulted from the retrospective design.

Miscellaneous

In a Danish population-based study with 21,152 patients, Holmes et al. reported that the recurrence risk of colorectal cancer was highest in the first three years of follow-up.³⁹ They also reported that patients had 55 years old or younger had increased risk of recurrence. In our study, age showed non-significant findings. Different cancer stages and populations at diagnosis might contribute this finding (the study include stage I-III colorectal cancers).

A cohort study with 1,857 patients reported that pre-operative anemia (Hemoglobin level < 7.5 mmol/L in women and < 8.0 mmol/L in men) was associated with poor 3-year overall survival and higher local recurrence rate in multivariable analysis model.⁴⁰ Regarding to BMI, a retrospective analysis showed more conversion to open surgery and higher rate of surgical complications in a large case series of 1464 patients.⁴¹

Another retrospective study reported that patients had overweight (BMI ≥ 35 kg/m²) or underweight (BMI < 18.5 kg/m²) had reduced overall survival and higher rates of distant metastases in comparison to patients with normal bodyweight.⁴² Due to the small sample size as well as non-significant hazard ratio, more studies should be reviewed. Due to different selected patient groups, our study showed non-significant findings on hemoglobin level or BMI.

Limitations

Our study had some limitations. Though we used cox-regression hazard model carefully, retrospective design possibly made causal fallacy. The patient records were not perfectly complete, for example, there were some few laboratory data losses, and we had no data of microsatellite instability or other biomarkers including KRAS, or BRAF. However, KRAS mutation may be linked with higher chance of distant metastasis.⁴³

Conclusions

In this analysis for early stage rectal cancer, “Pre-operative CEA ≥ 5 (ng/mL)” and “Early post-operative morbidity” were significant risk factors for distant metastasis; “Resection margin ≤ 0.1 (cm)” was a significant risk factor for local recurrence. “Lymphovascular invasion” and “Tumor diameter ≥ 3 (cm)” had borderline significance. Overall, there were 18 (5.1%) distant metastases and 8 (2.3%) local recurrences in our study. We suggest carefully follow-up plan for those who has early stage rectal cancer and high-risk factors. Further study on follow-up strategy and adjuvant treatment are needed to achieve better survival.

Abbreviations

LAR: low anterior resection, LVI: lympho-vascular invasion, PNI: perineural invasion BMI: body mass index, CEA: carcinoembryonic antigen, DAV:

distance from anal verge, CCRT: concurrent chemoradiation, DFS: disease-free survival, HR: hazard ratio, TEM: trans-anal endoscopic microsurgery, CT: computed tomography, MRI: magnetic resonance imaging.

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References

1. Watanabe T, Muro K, Ajioka Y, Hashiguchi Y, Ito Y, Saito Y, Hamaguchi T, Ishida H, Ishiguro M, Ishihara S, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2016 for the treatment of colorectal cancer. *Int J Clin Oncol* 2018;23(1):1-34.
2. Paun BC, Cassie S, MacLean AR, Dixon E, Buie WD. Post-operative complications following surgery for rectal cancer. *Ann Surg* 2010;251(5):807-18.
3. Emmertsen KJ, Laurberg S, Rectal Cancer Function Study G. Impact of bowel dysfunction on quality of life after sphincter-preserving resection for rectal cancer. *Br J Surg* 2013;100(10):1377-87.
4. Bregendahl S, Emmertsen KJ, Lindegaard JC, Laurberg S. Urinary and sexual dysfunction in women after resection with and without preoperative radiotherapy for rectal cancer: a population-based cross-sectional study. *Colorectal Dis* 2015;17(1):26-37.
5. Emmertsen KJ, Laurberg S. Low anterior resection syndrome score: development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. *Ann Surg* 2012;255(5):922-8.
6. Lynn PB, Renfro LA, Carrero XW, Shi Q, Strombom PL, Chow O, Garcia-Aguilar J. Anorectal function and quality of life in patients with early stage rectal cancer treated with chemoradiation and local excision. *Dis Colon Rectum* 2017;60(5):459-68.
7. Reissfelder C, Rahbari NN, Koch M, Ulrich A, Pfeilschifter I, Waltert A, Muller SA, Schemmer P, Buchler MW, Weitz J. Validation of prognostic scoring systems for patients undergoing resection of colorectal cancer liver metastases. *Ann Surg Oncol* 2009;16(12):3279-88.
8. Kumar R, Price TJ, Beeke C, Jain K, Patel G, Padbury R, Young GP, Roder D, Townsend A, Bishnoi S, et al. Colorectal cancer survival: an analysis of patients with metastatic disease synchronous and metachronous with the primary tumor. *Clin Colorectal Cancer* 2014;13(2):87-93.
9. Brenner H, Kloor M, Pox CP. Colorectal cancer. *Lancet* 2014;383(9927):1490-502.
10. Rahbari NN, Carr PR, Jansen L, Chang-Claude J, Weitz J, Hoffmeister M, Brenner H. Time of metastasis and outcome in colorectal cancer. *Ann Surg* 2019;269(3):494-502.
11. Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. *CA Cancer J Clin* 2014;64(2):104-17.
12. Rich T, Gunderson LL, Lew R, Galdibini JJ, Cohen AM, Donaldson G. Patterns of recurrence of rectal cancer after potentially curative surgery. *Cancer* 1983;52(7):1317-29.
13. Leijssen LGJ, Dinaux AM, Kinutake H, Bordeianou LG, Berger DL. Do stage I colorectal cancers with lymphatic invasion require a different postoperative approach? *J Gastrointest Surg* 2018.
14. Costi R, Santi C, Bottarelli L, Azzoni C, Zarzavadjian Le Bian A, Ricco M, Sarli L, Silini EM, Violi V. Anastomotic recurrence of colon cancer: genetic analysis challenges the widely held theories of cancerous cells' intraluminal implantation and metachronous carcinogenesis. *J Surg Oncol* 2016;114(2):228-36.
15. Cho WK, Choi DH, Park HC, Park W, Yu JI, Park YS, Park JO, Lim HY, Kang WK, Kim HC, et al. Elevated CEA is associated with worse survival in recurrent rectal cancer. *Onco-target* 2017;8(62):105936-41.
16. Lee JH, Lee JL, Park IJ, Lim SB, Yu CS, Kim JC. Identification of recurrence-predictive indicators in stage I colorectal cancer. *World J Surg* 2017;41(4):1126-33.
17. Sohn DK, Han KS, Kim BC, Hong CW, Chang HJ, Baek JY, Kim MJ, Park SC, Oh JH, Kim DY. Endoscopic assessment of tumor regression after preoperative chemoradiotherapy as a prognostic marker in locally advanced rectal cancer. *Surg Oncol* 2017;26(4):453-9.
18. Gunawardene A, Larsen P, Shekhouh A, Dennett E. Pre-operative carcinoembryonic antigen predicts survival following colorectal cancer surgery with curative intent. *ANZ J Surg* 2018;88(12):1311-5.
19. Huang EY, Chang JC, Chen HH, Hsu CY, Hsu HC, Wu KL. Carcinoembryonic antigen as a marker of radioresistance in colorectal cancer: a potential role of macrophages. *BMC Cancer* 2018;18(1):321.
20. Chung MJ, Nam TK, Jeong JU, Kim SH, Kim K, Jang HS, Jeong BK, Lee JH. Can serum dynamics of carcinoembryonic

- antigen level during neoadjuvant chemoradiotherapy in rectal cancer predict tumor response and recurrence? A multi-institutional retrospective study. *Int J Colorectal Dis* 2016;31(9):1595-601.
21. Yamano T, Yamauchi S, Tsukamoto K, Noda M, Kobayashi M, Hamanaka M, Babaya A, Kimura K, Son C, Imada A, et al. Evaluation of appropriate follow-up after curative surgery for patients with colorectal cancer using time to recurrence and survival after recurrence: a retrospective multicenter study. *Oncotarget* 2018;9(39):25474-90.
 22. Wang S, Liu J, Wang S, Zhao H, Ge S, Wang W. Adverse effects of anastomotic leakage on local recurrence and survival after curative anterior resection for rectal cancer: a systematic review and meta-analysis. *World J Surg* 2017;41(1):277-84.
 23. Zeng WG, Liu MJ, Zhou ZX, Wang ZJ. A distal resection margin of ≤ 1 mm and rectal cancer recurrence after sphincter-preserving surgery: the role of a positive distal margin in rectal cancer surgery. *Dis Colon Rectum* 2017;60(11):1175-83.
 24. Halverson AL, Morris AM, Cleary RK, Chang GJ. For patients with early rectal cancer, does local excision have an impact on recurrence, survival, and quality of life relative to radical resection? *Ann Surg Oncol* 2019.
 25. Allaix ME, Arezzo A, Morino M. Transanal endoscopic microsurgery for rectal cancer: T1 and beyond? An evidence-based review. *Surg Endosc* 2016;30(11):4841-52.
 26. Lee L, Kelly J, Nassif GJ, Atallah SB, Albert MR, Shridhar R, Monson JRT. Chemoradiation and local excision for T2N0 rectal cancer offers equivalent overall survival compared to standard resection: a national cancer database analysis. *J Gastrointest Surg* 2017;21(10):1666-74.
 27. Jawitz OK, Adam MA, Turner MC, Gilmore BF, Migaly J. Neoadjuvant chemoradiation followed by transanal local excision for T2 rectal cancer confers equivalent survival benefit as traditional transabdominal resection. *Surgery* 2019.
 28. Cutting JE, Hallam SE, Thomas MG, Messenger DE. A systematic review of local excision followed by adjuvant therapy in early rectal cancer: are pT1 tumours the limit? *Colorectal Dis* 2018;20(10):854-63.
 29. Sasaki T, Ito Y, Ohue M, Kanemitsu Y, Kobatake T, Ito M, Moriya Y, Saito N. Postoperative chemoradiotherapy after local resection for high-risk T1 to T2 low rectal cancer: results of a single-arm, multi-institutional, phase II clinical trial. *Dis Colon Rectum* 2017;60(9):914-21.
 30. O'Neill CH, Platz J, Moore JS, Callas PW, Cataldo PA. Transanal endoscopic microsurgery for early rectal cancer: a single-center experience. *Dis Colon Rectum* 2017;60(2):152-60.
 31. Sajid MS, Farag S, Leung P, Sains P, Miles WF, Baig MK. Systematic review and meta-analysis of published trials comparing the effectiveness of transanal endoscopic microsurgery and radical resection in the management of early rectal cancer. *Colorectal Dis* 2014;16(1):2-14.
 32. Morino M, Risio M, Bach S, Beets-Tan R, Bujko K, Panis Y, Quirke P, Rembacken B, Rullier E, Saito Y, et al. Early rectal cancer: the European Association for Endoscopic Surgery (EAES) clinical consensus conference. *Surg Endosc* 2015;29(4):755-73.
 33. Smart CJ, Korsgen S, Hill J, Speake D, Levy B, Steward M, Geh JI, Robinson J, Sebag-Montefiore D, Bach SP. Multi-centre study of short-course radiotherapy and transanal endoscopic microsurgery for early rectal cancer. *Br J Surg* 2016;103(8):1069-75.
 34. Stornes T, Wibe A, Nesbakken A, Myklebust TA, Endreseth BH. National early rectal cancer treatment revisited. *Dis Colon Rectum* 2016;59(7):623-9.
 35. Matsuda T, Fukuzawa M, Uraoka T, Nishi M, Yamaguchi Y, Kobayashi N, Ikematsu H, Saito Y, Nakajima T, Fujii T, et al. Risk of lymph node metastasis in patients with pedunculated type early invasive colorectal cancer: a retrospective multicenter study. *Cancer Sci* 2011;102(9):1693-7.
 36. Chang HC, Huang SC, Chen JS, Tang R, Changchien CR, Chiang JM, Yeh CY, Hsieh PS, Tsai WS, Hung HY, et al. Risk factors for lymph node metastasis in pT1 and pT2 rectal cancer: a single-institute experience in 943 patients and literature review. *Ann Surg Oncol* 2012;19(8):2477-84.
 37. Ha RK, Han KS, Sohn DK, Kim BC, Hong CW, Chang HJ, Hyun JH, Kim MJ, Park SC, Oh JH. Histopathologic risk factors for lymph node metastasis in patients with T1 colorectal cancer. *Ann Surg Treat Res* 2017;93(5):266-71.
 38. Dev K, Veerenderkumar KV, Krishnamurthy S. Incidence and predictive model for lateral pelvic lymph node metastasis in lower rectal cancer. *Indian J Surg Oncol* 2018;9(2):150-6.
 39. Holmes AC, Riis AH, Erichsen R, Fedirko V, Ostfeld EB, Vyberg M, Thorlacius-Ussing O, Lash TL. Descriptive characteristics of colon and rectal cancer recurrence in a Danish population-based study. *Acta Oncol* 2017;56(8):1111-9.
 40. Bruns ERJ, Borstlap WAA, van Duijvendijk P, van der Zaag-Loonen HJ, Buskens CJ, van Munster BC, Bemelman WA, Tanis PJ. The association of preoperative anemia and the postoperative course and oncological outcome in patients undergoing rectal cancer surgery: a Multicenter Snapshot Study. *Dis Colon Rectum* 2019.
 41. Bell S, Kong JC, Wale R, Staples M, Oliva K, Wilkins S, Mc Murrick P, Warrier SK. The effect of increasing body mass index on laparoscopic surgery for colon and rectal cancer. *Colorectal Dis* 2018;20(9):778-88.
 42. Kalb M, Langheinrich MC, Merkel S, Krautz C, Brunner M, Benard A, Weber K, Pilarsky C, Grutzmann R, Weber GF. Influence of body mass index on long-term outcome in patients with rectal cancer-a single centre experience. *Cancers (Basel)* 2019;11(5).
 43. Sideris M, Moorhead J, Diaz-Cano S, Haji A, Papagrigroriadis S. KRAS mutant status may be associated with distant recurrence in early-stage rectal cancer. *Anticancer Res* 2017;37(3):1349-57.

Supplement

Supplementary Table 1. Resection margin, operation methods, and local recurrence

Resection margin (cm)	≤ 0.1	0.2-0.5	0.6-2.0	> 2.0
Local excision	32	23	3	0
LAR	11	37	154	64
APR	0	0	7	14
Subtotal colectomy	1	1	0	0
Hartmann's operation	1	1	0	1
Total number	45	62	164	79
Local recurrence	4	1	2	1

LAR: low anterior resection; APR: abdomino-perineal resection.

In this supplementary table, there were 4 patients (2 received LE, 2 received LAR) had local recurrences. Despite very close resection margin, none of them received adjuvant therapy (including CCRT or chemotherapy). Local excision was thought to have higher chance of local recurrence due to close resection margin, however, 58 patients who received local excision had similar local recurrence rate with those received other surgical methods. Nearly half of these 58 patients received adjuvant therapy, which might bring survival benefits in this study.

原 著

早期中低位直腸癌術後局部復發及遠端轉移之危險因子分析

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目的 對於接受根治性手術的早期直腸癌病人來說，疾病的復發並不常見，也對給予治療的醫師帶來挫折感。本研究討論遠端轉移及局部復發，企圖分別找出兩種不同復發方式的危險因子。

方法 篩選於 2005 年至 2016 年間，林口長庚醫院接受局部切除或廣泛切除的根治性手術的病人，且其病理腫瘤分期為 T1 或 T2。危險因子藉由 Kaplan-Meier 存活分析辨識，經 Log-rank test 檢定 p 值 < 0.1 者進入多因子迴歸分析，結果以風險比例 (Hazard Ratio) 呈現。

結果 本研究共有 350 個病例，術後追蹤期中位數為 73.8 月。「術前癌胚抗原 (CEA) 大於等於 5 (ng/mL)」或「術後 30 天內有併發症」為遠端轉移的顯著危險因子；「腫瘤切除邊界小於等於 0.1 公分」為局部復發的顯著危險因子。其餘「淋巴血管侵犯」或「腫瘤直徑大於等於 3 公分」也有較高風險比例，但未達顯著統計差異。

結論 對早期直腸癌來說，復發並不常見。就本研究發現的危險因子，或能提供有此類危險因子的病人，審慎的調整追蹤策略。對於輔助性治療的研究，也能提供有價值的啟發作用。

關鍵詞 早期直腸癌、遠端復發、局部復發、危險因子分析。

Original Article

Comparison among LigaSure, Harmonic Scalpel, and Conventional Hemorrhoidectomy for Symptomatic Hemorrhoids

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Key Words

LigaSure;

Harmonic Scalpel;

Hemorrhoidectomy

Purpose. This study aimed to compare the short-term outcomes of LigaSure and Harmonic Scalpel hemorrhoidectomy with those of conventional hemorrhoidectomy.

Methods. We assessed patients with Grade III or IV hemorrhoids who underwent LigaSure, Harmonic Scalpel, or conventional hemorrhoidectomy from July 2018 to January 2019. A total of 50 patients were included in this study.

Results. The patients were divided into three groups: conventional ($n = 18$), LigaSure ($n = 16$), and Harmonic Scalpel hemorrhoidectomy ($n = 16$). The median operation time was 17.5 min for the LigaSure hemorrhoidectomy group, 18.75 min for the Harmonic Scalpel hemorrhoidectomy group, and 28.89 min for the conventional hemorrhoidectomy group ($p < 0.001$). Further, intraoperative blood loss and pain scores were significantly lower in the LigaSure and Harmonic Scalpel hemorrhoidectomy groups than in the conventional hemorrhoidectomy group ($p < 0.001$). The median number of analgesic injections used during admission and hospital days was lower in the LigaSure and Harmonic Scalpel hemorrhoidectomy groups than in the conventional hemorrhoidectomy group ($p < 0.05$). However, no significant difference was observed in terms of the incidence of early postoperative complications.

Conclusions. LigaSure and Harmonic Scalpel hemorrhoidectomy provide a superior alternative to conventional hemorrhoidectomy owing to shorter operation time and length of hospital stay as well as lower postoperative pain, volume of blood loss, and analgesic requirements.

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Hemorrhoids are an extremely common condition defined as the symptomatic enlargement and protrusion of the anal cushions.¹ However, there are no statistical data available about the incidence of hemorrhoids in Taiwan. According to an epidemiological study conducted in the USA, 4%-5% of adults develop hemorrhoids, with the highest prevalence be-

ing between 45 and 65 years.²

Conservative treatment is often sufficient for early-stage hemorrhoids (Grades I and II). However, in late-stage hemorrhoids (Grades III and IV), surgical treatment is usually required.

The most effective hemorrhoidectomy techniques include the Milligan-Morgan open hemorrhoidectomy

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and Ferguson closed hemorrhoidectomy. These methods are similar and considered conventional methods.^{3,4}

In conventional hemorrhoidectomy, hemorrhoidal tissues are removed using a scalpel and electrocautery and the pedicle is ligated. The most significant complications of hemorrhoid surgery are postoperative pain and bleeding.⁵ Postoperative pain is related to the surgical incisions, anal mucosa suturing, use of cautery, and possible surgical-site infection.⁶

In recent years, many surgical facilities have been established owing to technological developments. To date, hemorrhoidectomies are performed with novel instruments such as bipolar electrothermal devices, ultrasonic scalpels, and circular staplers. The evolution of techniques and equipment has resulted in decreased pain and number of complications, such as bleeding, after hemorrhoidectomy.

The Harmonic Scalpel is an energy source, which uses ultrasonic vibrations at a frequency of 55.5 KHz and simultaneously cuts and coagulates up to 2 mm of blood vessels. The Harmonic Scalpel is advantageous because it causes extremely minimal lateral thermal injury to tissues. Decreased lateral thermal injury (< 1.5 mm) at the surgical site results in decreased postoperative pain.⁷

The LigaSure vessel-sealing system is a bipolar electrothermal device that seals blood vessels with a calculated arrangement of pressure and radio frequency. It ensures complete coagulation of blood vessels up to 7 mm in diameter with minimal surrounding thermal spread and limited tissue charring. Sealing of hemorrhoidal tissues between the LigaSure forceps is assumed to be achieved with minimal collateral thermal spread and limited tissue charring, leading to a reduced incidence of postoperative pain.

Hemorrhoidectomy using these two energy devices might lead to better outcomes. Thus, performing hemorrhoidectomy with these two energy devices leads to lower operation time, and such devices provide a less painful alternative to conventional techniques. The present study aimed to compare the outcomes of patients with Grade III or IV hemorrhoids who underwent hemorrhoidectomy using these energy devices or the conventional closed technique.

Materials and Methods

Study design

This retrospective study was conducted at the Department of Surgery of Chia-Yi Christian Hospital. In total, 50 patients with symptomatic Grade III or IV hemorrhoids who underwent surgery conducted by a single surgeon between July 2018 and January 2019 were enrolled. The patients were divided into three groups: conventional (n = 18), LigaSure (n = 16), and Harmonic Scalpel hemorrhoidectomy (n = 16). The exclusion criteria were as follows: individuals with thrombosed/strangulated hemorrhoids, concomitant perianal disease, history of recurrent perianal surgery, those at risk of postoperative bleeding, and those unfit for surgery and anesthesia. One soaked 3 × 3 gauze is equivalent to 4 mL intraoperative blood loss. Patients who were receiving anticoagulant medication or aspirin were instructed to stop their use 7 days prior to the surgery.

Surgery

All patients underwent preoperative laboratory tests, chest radiography, electrocardiography, and urinalysis. They were admitted to the hospital on the day of surgery. All patients used monosodium phosphate enema once before the surgery, and prophylactic antibiotics were injected before transporting the patients to the surgical room. All patients received spinal or general anesthesia according to the preference of the patient, surgeon, and anesthesiologist. The patients were placed in the jackknife position. Tapes were attached to both sides of the buttocks to expose the anus, and a Hill-Ferguson retractor was inserted into the anal canal to visualize the surgical field. The Ferguson closed technique was used. Hemorrhoidal pedicles originating above the dentate line to above the hemorrhoidal plexus were removed using a scalpel and electrocautery device; 4-0 vicryl suture was used to close the wound.

LigaSure hemorrhoidectomy with submucosal dissection was first performed with a skin incision created at the junction of the hemorrhoids and peri-

anal skin using a scalpel followed by dissection of the hemorrhoidal bundles off the underlying sphincters. A LigaSure handset was used for the dissected hemorrhoids up to their pedicles while ensuring that the underlying sphincters were not injured. The device was activated to seal the mucosal edges. A feedback-controlled sensor signaled the completion of coagulation, and the coagulated tissue was excised along the line of the coagulum. During hemorrhoidectomy using the Harmonic Scalpel, the hemorrhoidal tissue and its pedicle were excised up to the apex region without damaging the internal sphincter using vascular forceps. The hemorrhoidal mucosa and coagulated blood vessels of the hemorrhoid were excised with a Harmonic Scalpel, and mucosal suturing with 4-0 vicryl was performed.

Postoperative intervention

After the surgery, neomycin ointment was topically applied on the wound, which was covered by gauze. Then, the gauze was removed, and sitz baths were initiated on the postoperative day 1 for all patients. Further, a combination of 37.5 mg oral tramadol and 325 mg acetaminophen (Traceton) was orally administered at a regular dose if the patients had no contraindications. If a patient continued experiencing pain, 30 mg ketorolac was intravenously administered. In cases of severe bladder distention or if a patient failed to urinate 8 h after the surgery, an intermittent Foley catheter was inserted. Once stable and

when the wound stopped bleeding or oozing, the patients were discharged. We measured and recorded rest pain using the visual analog scale (VAS), volume of blood loss, and any occurrence of urinary retention. The VAS pain score ranges from 0 (indicating no pain) to 10 (indicating severe pain). All patients were instructed to grade the severity of pain on a scale of 0-10 in the evening of the surgery day (day 0), next day (day 1), and after a week during follow-up (day 7).

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences software version 16 (SPSS Inc., Chicago, IL, USA). A *p*-value of < 0.05 was considered statistically significant. Continuous and categorical variables were compared using the Kruskal-Wallis and chi-square test, respectively. One-way analysis of variance was used to compare the three groups in terms of age.

Results

The characteristics of 50 symptomatic patients with Grade III or IV hemorrhoids are summarized in Table 1. Among the patients, 18 (36%) were men and 32 (64%) were women. The mean ages of the patients in the conventional, LigaSure, and Harmonic Scalpel hemorrhoidectomy groups were 47.33 ± 10.13 , 47.81 ± 9.70 , and 49.13 ± 10.12 years, respectively. No sig-

Table 1. Characteristics of the patients in terms of type of operation

	Type of operation			<i>p</i> -value
	Conventional hemorrhoidectomy group n = 18	LigaSure hemorrhoidectomy group n = 16	Harmonic Scalpel hemorrhoidectomy group n = 16	
Age (years) mean \pm SD	47.33 \pm 10.13	47.81 \pm 9.70	49.13 \pm 10.12	0.985
Sex				0.888
Male	7 (38.89)	5 (31.25)	6 (37.50)	
Female	11 (61.11)	11 (68.75)	10 (62.50)	
Grade				0.913
III	4 (22.22)	4 (25.00)	3 (18.75)	
IV	14 (77.78)	12 (75.00)	13 (81.25)	

SD, standard deviation.

nificant difference was observed among the three groups in terms of age, sex, and grade of hemorrhoids. Table 2 shows the perioperative details and postoperative outcomes of the three groups. The median operation time of the conventional, LigaSure, and Harmonic Scalpel hemorrhoidectomy groups was 28.89 ± 6.76 , 17.50 ± 3.16 , and 18.75 ± 2.24 min, respectively, indicating significantly longer operation time in the conventional hemorrhoidectomy group than in the other groups ($p < 0.001$). Intraoperative blood loss was significantly higher in the conventional hemorrhoidectomy group than in the LigaSure and Harmonic Scalpel hemorrhoidectomy groups (28.06 ± 7.30 , 13.44 ± 3.01 , and 12.50 ± 2.58 mL, respectively; $p < 0.001$). The VAS pain scores on postoperative days 0, 1, and 7 were significantly higher in the conventional hemorrhoidectomy group than in the other groups ($p < 0.001$). In addition, the number of parenteral analgesic injections was higher and the length of hospital stay was significantly longer in the conventional hemorrhoidectomy group than in the other groups ($p < 0.05$). However, the operation time, volume of blood loss, postoperative VAS pain score, length of hospital stay, and number of parenteral analgesic injections did

not significantly differ between the LigaSure and Harmonic Scalpel hemorrhoidectomy groups. Postoperative complications were observed in 2 (12.5%) patients each in the LigaSure and Harmonic Scalpel hemorrhoidectomy groups and in 5 (27.78%) in the conventional hemorrhoidectomy group. Urinary retention requiring temporary catheterization was observed in 1 (6.25%) patient in the LigaSure and Harmonic Scalpel hemorrhoidectomy groups and 3 (16.67%) in the conventional hemorrhoidectomy group. Bleeding in the early postoperative period (within 7 days of surgery) developed in 1 (6.25%) patient in the LigaSure and Harmonic Scalpel hemorrhoidectomy groups and 2 (11.11%) in the conventional hemorrhoidectomy group. All patients who presented bleeding recovered after conservative treatment, and none of them required further surgical intervention. Postoperative complications among these three groups did not show significant difference.

Discussion

Hemorrhoids are an extremely common anorectal

Table 2. Operative and postoperative parameters

	Type of operation			<i>p</i> -value
	Conventional hemorrhoidectomy group n = 18	LigaSure hemorrhoidectomy group n = 16	Harmonic Scalpel hemorrhoidectomy group n = 16	
Operation time (min) mean \pm SD	28.89 ± 6.76	17.50 ± 3.16^a	18.75 ± 2.24^a	< 0.001
Volume of blood loss	28.06 ± 7.30	13.44 ± 3.01^a	12.50 ± 2.58^a	< 0.001
VAS pain score				
Day 0	6.22 ± 0.81	4.44 ± 0.63^a	4.13 ± 0.72^a	< 0.001
Day 1	5.22 ± 0.88	3.38 ± 0.62^a	3.06 ± 0.44^a	< 0.001
Day 7	2.33 ± 0.84	1.44 ± 0.63^a	1.38 ± 0.50^a	< 0.001
Length of hospital stay	1.94 ± 0.64	1.44 ± 0.51^a	1.31 ± 0.48^a	0.004
Postoperative complication				
Hemorrhage				0.831
N	16 (88.89)	15 (93.75)	15 (93.75)	
Y	2 (11.11)	1 (6.25)	1 (6.25)	
Urinary retention				0.499
N	15 (83.33)	15 (93.75)	15 (93.75)	
Y	3 (16.67)	1 (6.25)	1 (6.25)	
Number of ketorolac injections	1.28 ± 0.46	0.94 ± 0.25^a	0.88 ± 0.34^a	0.006

SD, standard deviation.

^a *p*-value < 0.05 vs. conventional hemorrhoidectomy group.

disease defined as the symptomatic enlargement and distal displacement of the anal cushions. Globally, millions of individuals present this condition, and it is considered a major socioeconomic and medical issue. Approximately 10 million Americans present this condition annually, with a prevalence of 4.4%.⁸ However, there are no statistical data available about the incidence of hemorrhoids in Taiwan.

Several factors, including constipation and prolonged straining, are associated with symptomatic hemorrhoids. Distortion of the vascular channel, with destructive changes in the supporting connective tissue within the anal cushions, is a common finding in hemorrhoids.⁹

Hemorrhoids are extremely vascular submucosal cushions that generally lie along the anal canal in three columns: left lateral, right anterior and right posterior positions. Hemorrhoids play an important physiological role in protecting the anal sphincter muscles and reinforcing closure of the anal canal during moments involving increased abdominal pressure (e.g., coughing and sneezing) to prevent incontinence and provide 15%-20% of the anal canal resting pressure.¹⁰

Increase in abdominal pressure elevates the pressure in the inferior vena cava, causing these vascular cushions to engorge and prevent leakage. This tissue is also believed to help distinguish stool, liquid, and gas in the anal canal.¹⁰

Conventional hemorrhoidectomy techniques, including Milligan-Morgan open hemorrhoidectomy and Ferguson closed hemorrhoidectomy, are effective and suitable treatments for Grades III and IV hemorrhoids. However, these conventional surgeries can cause complications such as postoperative pain and bleeding.¹¹

The resulting pain-related complications after conventional hemorrhoidectomy are often the main factors that account for prolonged hospital stays and delayed recovery.

In the past few years, hemorrhoid surgeries conducted in newly developed facilities have resulted in less postoperative pain and bleeding as well as shorter operation time and hospital stay.^{12,13}

Circular stapling devices for prolapsed hemorrhoids have recently been introduced. However, these

devices have been criticized because they cannot treat the external component of hemorrhoids and skin tags. In addition, they are costly, and the procedure often leads to complications such as postoperative bleeding, rupture of the anastomotic site, pelvic sepsis, anastomotic stricture, and rectovaginal fistula.^{14,15}

When performing hemorrhoidectomy with energy devices, intraoperative bleeding is minimized and the visualization of the surgical field is better. Performing simultaneous resection and hemostasis reduces the operation time and related complications, such as postoperative bleeding, pain, and infection, by decreasing damage to the surrounding mucosal tissues. In contrast, when performing conventional hemorrhoidectomy, the surrounding mucosal tissues and blood vessels can be damaged during resection of the hemorrhoidal tissue, and the time to hemostasis of blood vessels and tissues may increase the operation time and risk of postoperative bleeding. In addition, several studies have reported that the use of the LigaSure or ultrasonic scalpel hemorrhoidectomy results in significantly shorter operation time and less postoperative bleeding than that of conventional hemorrhoidectomy.^{16,17}

The main finding of the present study is that Harmonic Scalpel and LigaSure hemorrhoidectomy obtained better results for the perioperative and postoperative parameters than conventional hemorrhoidectomy. Compared with the conventional Ferguson's method, LigaSure and Harmonic Scalpel hemorrhoidectomies lead to significantly shorter operation time ($p < 0.001$) and lower volume of blood loss ($p < 0.001$). The VAS pain scores at postoperative days 0, 1, and 7 were significantly lower in the LigaSure and Harmonic Scalpel hemorrhoidectomy groups than in the conventional hemorrhoidectomy group ($p < 0.001$). Further, the postoperative hospital stay and parenteral analgesic requirement were lower in the LigaSure and Harmonic Scalpel hemorrhoidectomy groups ($p < 0.05$). The incidence of early postoperative complications, such as hemorrhage and urinary retention, was higher in the conventional hemorrhoidectomy group than in the other groups, albeit the difference was not statistically significant. The incidence of early postoperative complication of LigaSure and Harmonic

Scalpel hemorrhoidectomy is comparable to that of conventional hemorrhoidectomy, without serious complications. After conservative management, all patients recovered uneventfully without subsequent surgical intervention.

Our study showed the pain control profile of LigaSure and Harmonic Scalpel hemorrhoidectomy to be superior to that of conventional hemorrhoidectomy. Moreover, the patients for whom such methods were used required fewer analgesic injections.

Similar results have been obtained in previous studies. For example, Chung et al.¹⁸ reported that Harmonic Scalpel hemorrhoidectomy is superior to bipolar scissors hemorrhoidectomy because it is associated with less postoperative pain and better patient satisfaction. Further, Wang et al.¹⁹ found that LigaSure hemorrhoidectomy is associated with significantly less postoperative pain and parenteral analgesic requirements than Ferguson hemorrhoidectomy.

LigaSure has been used in hemorrhoidectomy, and it has been compared with Harmonic Scalpel in a randomized controlled trial conducted by Kwok et al.,²⁰ which showed a significantly higher postoperative pain score, postoperative oral analgesic requirement, and operation time in the Harmonic Scalpel group. In this study, no significant difference was observed in terms of hospital stay, patient satisfaction score and complication rates. This difference could be explained by the relatively small number of patients included in their study, which is a factor that inhibits obtaining a more comprehensive conclusion.

The present study has some limitations. First, this was a nonrandomized retrospective study, which might have resulted in a baseline selection bias. Second, our follow-up period was extremely short; therefore, data about long-term outcomes were limited. Lastly, this study had a small sample size with only 50 patients. Thus, future studies with long follow-up periods that assess late complications must be conducted.

Conclusions

LigaSure and Harmonic Scalpel hemorrhoidectomy provide a superior alternative to conventional

hemorrhoidectomy because they result in shorter operation time and hospital stay as well as lower postoperative pain, volume of blood loss, and analgesic requirements. However, studies with long-term follow-up and larger sample size must be conducted.

References

1. Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. *World J Gastroenterol* 2012;18:2009-17.
2. Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation. An epidemiologic study. *Gastroenterology* 1990;98:380-6.
3. Milligan ET, Morgan CN, Jones LE, Office R. Surgical anatomy of the anal canal, and the operative treatment of hemorrhoids. *Lancet* 1937;230:1119-24.
4. Ferguson JA, Heaton JR. Closed hemorrhoidectomy. *Dis Colon Rectum* 1959;2:176-9.
5. Kwok SY, Chung CC, Tsui KK, Li MK. A double-blind randomized trial comparing ligature and harmonic scalpel hemorrhoidectomy. *Dis Colon Rectum* 2005;48:344-8.
6. Nicholson TJ, Armstrong D. Topical metronidazole (10 percent) decreases post hemorrhoidectomy pain and improves healing. *Dis Colon Rectum* 2004;47:711-6.
7. Hulme-Moir M, Bartolo DC. Hemorrhoids. *Gastroenterol Clin North Am* 2001;30:183-97.
8. Sanchez C, Chinn BT. Hemorrhoids. *Clin Colon Rectal Surg* 2011;24:5-13.
9. Loder PB, Kamm MA, Nicholls RJ, Phillips RK. Hemorrhoids: pathology, pathophysiology and etiology. *Br J Surg* 1994;81:946-54.
10. Cintron J, Abacarian H. *Benign anorectal: hemorrhoids*. In: Wolff BG, Fleshman JW, Eds. *The ASCRS of Colon and Rectal Surgery*. New York, NY: Springer-Verlag, 2007:156-77.
11. Chen JS, You JF. Current status of surgical treatment for hemorrhoids--systematic review and meta-analysis. *Chang Gung Med J* 2010;33:488-500.
12. Jayne DG, Botterill I, Ambrose NS, Brennan TG, Guillo PJ, O'Riordain DS. Randomized clinical trial of Ligasure versus conventional diathermy for day-case haemorrhoidectomy. *Br J Surg* 2002;89:428-32.
13. Bulus H, Tas A, Coskun A, Kucukazman M. Evaluation of two hemorrhoidectomy techniques: harmonic scalpel and Ferguson's with electrocautery. *Asian J Surg* 2014;37:20-3.
14. Engel AF, Eijssbouts QA. Hemorrhoidectomy: painful choice. *Lancet* 2000;355:2253-4.
15. Ravo B, Amato A, Bianco V, Boccasanta P, Bottini C, Carriero A, et al. Complications after stapled hemorrhoidectomy: can they be prevented? *Tech Coloproctol* 2002;6: 83-8.

16. Palazzo FF, Francis DL, Clifton MA. Randomized clinical trial of LigasureTM versus open hemorrhoidectomy. *Br J Surg* 2002;89:154-7.
17. Jayne DG, Botterill I, Ambrose NS, Brennan TG, Guillou PJ, O'Riordain DS. Randomized clinical trial of LigasureTM versus conventional diathermy for day-case hemorrhoidectomy. *Br J Surg* 2002;89:428-32.
18. Chung CC, Ha JP, Tai YP, Tsang WW, Li MK. Double-blind, randomized trial comparing Harmonic Scalpel hemorrhoidectomy, bipolar scissors hemorrhoidectomy, and scissors excision: ligation technique. *Dis Colon Rectum* 2002;45:789-94.
19. Wang JY, Lu CY, Tsai HL, Chen FM, Huang CJ, Huang YS, et al. Randomized controlled trial of LigaSure with submucosal dissection versus Ferguson hemorrhoidectomy for prolapsed hemorrhoids. *World J Surg* 2006;30:482-6.
20. Kwok SY, Chung CC, Tsui KK, Li MK. A double-blind, randomized trial comparing Ligasure and Harmonic Scalpel hemorrhoidectomy. *Dis Colon Rectum* 2005;48:344-8.

原 著

使用組織凝集器 (LigaSure)、諧波刀 (Harmonic scalpel) 切除痔瘡與傳統痔瘡手術之比較

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目的 比較組織凝集器 (LigaSure)、諧波刀 (Harmonic scalpel) 切除痔瘡與傳統痔瘡手術的結果。

方法 收集並統計自 2018 年 7 月至 2019 年 1 月間，第三與第四級痔瘡使用組織凝集器、諧波刀手術及傳統痔瘡切除手術進行比較。共 50 位病人分為三組，比較彼此之間各方面的差別。

結果 使用組織凝集器及諧波刀進行痔瘡切除手術比傳統痔瘡手術能有效減少開刀時間及術中流血量；而且在住院天數、術後疼痛和術後施打止痛藥劑數用組織凝集器及諧波刀進行痔瘡切除手術也是明顯優於傳統痔瘡手術。

結論 使用組織凝集器 (LigaSure) 或諧波刀 (Harmonic Scalpel) 進行痔瘡切除手術，能夠比傳統手術達到更好的結果。

關鍵詞 組織凝集器 (LigaSure)、諧波刀 (Harmonic Scalpel)、痔瘡切除術。

Original Article

A Summary of 5 Crossover Trials on Sacral Nerve Stimulation for Fecal Incontinence

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Key Words

Sacral nerve stimulation;

Fecal incontinence;

Randomized controlled trial;

Cleveland Clinic incontinence score;

Fecal Incontinence Quality of Life Scale

Aims. Sacral nerve stimulation is a well-known treatment for fecal incontinence (FI). Standard reprogramming restores FI for some patients, but not all. A review of the literature was carried out to study this question.

Methods. A literature search was performed on Pubmed and Embase databases for all relevant articles till December 2018. Studies were included if they were crossover randomized clinical trial, evaluating the use of SNS on the patient with fecal incontinence and assessing at least one of the following end-points: the frequency of fecal incontinence episodes, Cleveland Clinic incontinence score (CCIS), Fecal Incontinence Quality of Life Scale (FIQLS) and the Wexner incontinence score. No restrictions on language or study size were made.

Results. Five RCT papers were identified and all of those were randomized crossover study. These included 176 patients and 104 participants. The average follow-up duration for these 5 studies was 3 months. Preliminary results suggest good outcome after permanent SNS implant. Results from the first three studies showed significantly reduced frequency of fecal incontinence episodes during the ON period. All three studies reported positive outcomes with the Cleveland Clinic incontinence score (CCIS) that were significantly improved in the ON period than the OFF period. Optimal pacemaker settings were individual, but a trend towards higher patient satisfaction and decreased incontinent episodes was evident for high-frequency stimulation (31 Hz/210 μ s) in comparison with the standard setting (14 Hz/210 μ s) ($p < 0.05$). Subsensory stimulation as low as 50% of the sensory threshold is as effective as stimulation at or above the sensory threshold. Finally, bilateral stimulation is not superior to standard unilateral stimulation in the short term.

Conclusions. The review suggests that SNS for fecal incontinence has significant improvement in fecal incontinence during the ON period with higher patient satisfaction and decreased incontinent episodes under high-frequency stimulation.

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Fecal incontinence (FI) is commonly defined as an involuntary loss control of the fecal material of liquid or solid stool.¹ FI remains a substantial therapeutic issue in many patients when medical treatment

fails and sphincter repair is unsuccessful. While variations exist regarding prevalence due to differences in survey methods, screening questions, definition and population studied. Biologic or artificial neosphincters

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are a therapeutic option in some cases, but these treatments have a significant failure rate and high associated morbidity.^{2,3}

Matzel and colleagues introduced Sacral nerve stimulation (SNS) therapy for fecal incontinence in 1995.⁴ SNS is a minimally invasive procedure that involves cutaneous electrical stimulation of the sacral nerve plexus via the S3 or S4 foramen, producing a physiological effect on the organs innervated by these nerves.⁵ Through neuromodulation, there is the potential to alter pelvic floor and anal sphincter function and afferent sensation eliciting a clinically beneficial effect. The concept of SNS can be traced back to the 19th century when the first clinical application was used by Brindley with high-voltage stimulation to treat patients with spinal cord injury.⁶ This was then adapted and applied to treat patients with urological dysfunction and the beneficial effect on fecal incontinence was also observed as well.⁷ Since then SNS has been demonstrated to have a beneficial effect in several retrospective trials^{4,8-15} and four prospective crossover trials.¹⁶⁻¹⁹

Neurostimulation is one of the fastest growing areas of medicine with application that significantly changed the treatment paradigm for many patients over the past decades. Study has shown that 80% of patients with fecal incontinence undergoing SNS had more than fifty percent improvement in their symptoms.²⁰ Long-term results have even shown a long-term maintenance rate of 71% in patients after permanent implant, with half of them having full continence.²¹ It is now considered the first-line surgical treatment option for the majority of adults with FI in whom medical treatments have failed to do the work.²²

Although sacral nerve stimulation has become an important tool for the treatment of fecal incontinence, on the other hand, the mechanism remains unclear and inter-individual differences do exist. This systematic review will look at cross-over studies on the use of SNS on patients with fecal incontinence and its effect on their quality of life.

Method

A literature search was performed on PubMed and

Embase for all relevant articles. The following keywords were used in various combinations to conduct the search: ‘sacral nerve stimulation’, ‘SNS’, ‘sacral nerve modulation’, ‘fecal incontinence’, ‘faecal incontinence’, and ‘crossover’. This comprehensive search used Boolean operator “OR” for expanding sensitivity and applied Boolean operator “AND” for specifying the result on this study topic. The search did not restrict the language or date, and the search strategy was completed on September 2018. All studies which were identified in this search were screened by investigators according to PRISMA guideline. The investigators screened title and abstract to include potential references and reviewed full-text to exclude the not eligible references. Our exclude criteria were Different type of device, Non-adult, Non-RCT, Different disease entity and Different target. After study selection, the investigators evaluated the quality of the eligible studies using Cochrane Risk of Bias Tool.

Patients with fecal incontinence on SNS were assessed at least one of the following end-points: the frequency of fecal incontinence episodes, Cleveland Clinic incontinence score (CCIS), Fecal Incontinence Quality of Life Scale (FIQLS) and the Wexner incontinence score.

Results

1726 studies were identified in the initial search and reviewed. 1698 studies were excluded due to non-randomized control trial. Nine repeated studies were excluded. Fourteen studies were on use of SNS on fecal continence and therefore were deemed irrelevant to this review by both authors. The remaining five trials included a total of 176 patients (Fig. 1). Among these patients, however, only 104 patient agreed to be enrolled for analysis. The characteristics of these studies are shown in Table 1.

In 2005,¹⁶ the first double-blind multicenter prospective randomized study reported by Leroi et al. examined the effectiveness of cross-over sacral nerve stimulation in patients with fecal incontinence. A total of 27 patients was enrolled. Twenty-four patients (89%) were self-reported to have improvement during

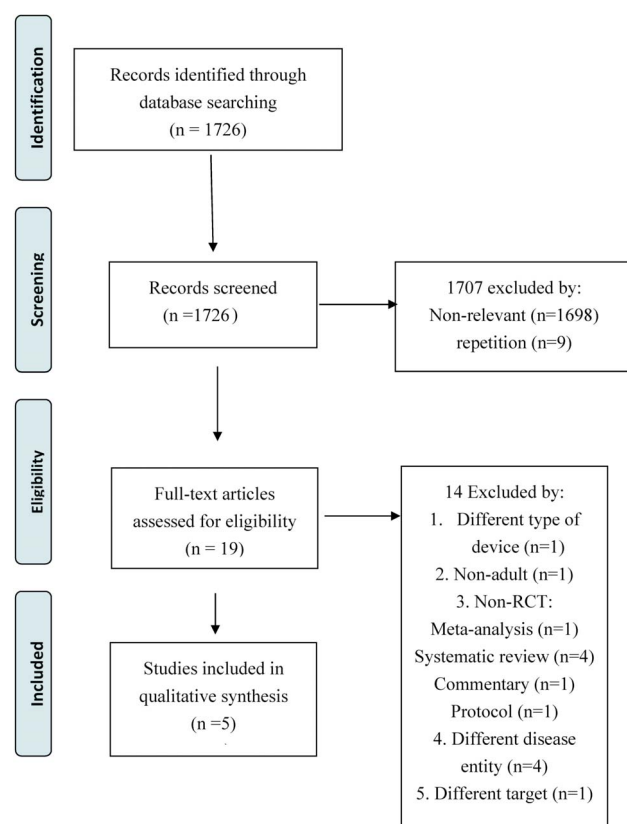


Fig. 1. PRISMA flow diagram.

the ON crossover period in comparison with 17 (63%) during the OFF period. Patients also felt that there was a significant improvement of their FIQOL. Cleveland Clinic incontinence score (CCIS) improved during postimplantation ($p < 0.002$) and final visits ($p < 0.0004$). Treatment details of permanent SNS implant are shown in Table 2. Four patients (0.1%) could not decide if they had improved or not ($p < 0.02$). Results of patients choice of stimulation (stimulation ON or OFF at the end of crossover), are shown in Table 3. Patients' choice for stimulation ON could be justified by a more marked symptomatic improvement during the ON than the OFF crossover period. That was not the case for those who had chosen the OFF stimulation.

A total of 16 patients was enrolled in the Kahlke et al. study.¹⁹ At the time of stimulator implantation, the mean age \pm SD was 55.5 ± 11.8 years. SNS led to a marked reduction in the mean frequency of FI episodes and the number of bowel movements per week during the ON period in comparison to the OFF period ($p = 0.004$). FI episodes decreased significantly from 18 ± 19.6 (mean \pm SD) at baseline to 1.1 ± 1.6 after implantation ($p = 0.003$) and remained at the low

Table 1. Characteristics of the studies

Study	Design	Data	No. of patients (enrolled)	Age	Gender M/F
Anne-Marie Leroi et al.	Multicenter Double-blind Crossover study	February 2000 to February 2003	34 (27)	57 ^a	3/31
Volker Kahlke et al.	Single-center Prospective randomized Crossover study	February 2012 to December 2012	45 (16)	55.5 ^b	12/33
J.Duelund-Jakobsen et al. (2012)	Single-center Double-blind Randomized Crossover study	July to September 2010	35 (15)	54.2 ^b	0/15
J.Duelund-Jakobsen et al. (2013)	Single-center Blinded Randomized Crossover study	January to April 2010	27 (19)	59.5 ^b	1/18
J.Duelund-Jakobsen et al. (2015)	Single-center Single-blinded Randomized Crossover study	May 2009 to June 2012.	35 (27)	63 ^a	2/25

^a Median; ^b Mean.

Table 2. Treatment details of permanent SNS implant

Study	No. of patients	No. patients (enrolled)	SNS lead	Test period	Follow-up duration
Anne-Marie Leroi et al.	34	27	quadripolar	1 month	3 months
Volker Kahlke et al.	45	16	quadripolar	3 weeks	3 months
J. Duelund-Jakobsen et al. (2012)	35	15	ND	3 weeks	3 months
J. Duelund-Jakobsen et al. (2013)	27	19	ND	3 weeks	3 months
J. Duelund-Jakobsen et al. (2015)	35	27	quadripolar	4 weeks	3 months

Table 3. Results of the Cleveland Clinic incontinence score and changes in the number of fecal incontinence episodes per week

Study	No. of patients	No. patients (enrolled)	Frequency of FI/week			Frequency of defecation/week			Cleveland clinic incontinent score (CCIS)		
			OFF			ON			OFF		
			0	14 Hz/ 210 μ s	31 Hz/ 210 μ s	0	14 Hz/ 210 μ s	31 Hz/ 210 μ s	0	14 Hz/ 210 μ s	31 Hz/ 210 μ s
Anne-Marie Leroi et al.	34	27	3.5 (0-10) ^b	0.5 (0-11) ^b	ND	11.7 (7-32) ^b	10.6 (7-37) ^b	ND	13 (11-18) ^b	10 (3-17) ^b	ND
Volker Kahlke et al.	45	16	8.4 \pm 8.7	1 \pm 1.7	ND	18.2 (8.7) ^a	10.9 (4.1) ^a	ND	14.6 (4.6) ^a	8.7 (3.6) ^a	ND
J. Duelund-Jakobsen et al. (2012)	35	15	ND (6.2) ^{a,c}	8.7 (7.2) ^{a,c}	6.4 (7.2) ^{a,c}	ND (32.1) ^{a,c}	44.1 (29.6) ^{a,c}	38.3 (29.6) ^{a,c}	ND (2.9) ^a	11.6 (3.8) ^a	11.1 (3.8) ^a

^a Mean \pm standard deviation; ^b Median (range); ^c Three weeks.

level of 1 ± 1.7 throughout the ON period, but increased significantly in the OFF period to 8.4 ± 8.7 . During the final period, FI episodes remained at a low 0.3 ± 0.5 . CCIS fell from 16 ± 4.6 at baseline to 5.1 ± 1.3 after implantation ($p < 0.0001$).

Fifteen patients were enrolled in J. Duelund-Jakobsen et al. (2012) study.¹⁸ Their mean age was 54.2 ± 9.2 (mean \pm SD) years and the duration of fecal incontinence before SNS therapy was 14.2 ± 10.2 (mean \pm SD) years. Significant improvement was seen in three of four subdomains in the FIQLS. Decreased number of incontinence episodes dropped from 11.7 (10.8) to 4.8 (4.5) per 3 weeks ($p = 0.011$) and improvements were maintained after 3 months of follow-up. The mean CCIS dropped from a baseline of 16.2 ± 3.3 (mean \pm SD) to final score of 13.5 ± 2.5 (mean \pm SD). After an initial period of successful treatment all patients had gradual loss of efficacy and reported dissatisfaction during later follow-up (mean 57.1 ± 27 [mean \pm SD] months after implantation of SNS). There was a trend towards higher patient satisfaction and improved outcome was observed for high-frequency stimulation (31 Hz/210 μ s) in 8 out 15 patients (Table 3).

Nineteen patients were enrolled in J. Duelund-Jakobsen et al (2013) randomized crossover study²³ with a mean follow-up of 51.7 ± 29.9 months, aimed to investigate if stimulation at 75% or 50% of the sensory threshold would be as effective as stimulation at the sensory threshold for fecal incontinence.

The results showed that the mean FI episodes per 3 weeks decreased from pre-SNS therapy significantly ($p < 0.001$). Decreasing the stimulation amplitude to as low as 50% of the subsensory threshold (ST) did not affect the overall number of incontinent episodes ($p = 0.078$). Decreasing the stimulation amplitude to 50% of the sensory threshold did not change the Wexner score when compared with the study baseline ($p = 0.581$).

Twenty-seven bilaterally implanted patients were enrolled in J. Duelund-Jakobsen et al. (2015) randomized crossover study,²⁴ aiming to investigate efficiency of bilateral sacral nerve stimulation over unilateral stimulation for fecal incontinence.

The results showed that bilateral SNS therapy for fecal incontinence is not superior to standard unilateral stimulation in the short term. The median number

of episodes of FI per 3 weeks significantly decreased and the Wexner score incontinence improved dramatically. Overall, the differences between unilateral right or unilateral left and bilateral stimulation were non-significant, for FI episodes ($p = 0.3$) and for Wexner incontinence score ($p = 0.9$) (Table 4).

Discussion

Fecal incontinence significantly impairs quality of life, affecting nearly all aspects of life. There were few randomized trials (ON vs. OFF stimulation) reported on the effect of SNS for the treatment. This systematic review demonstrates the outcome of 58 patients who had undergone SNS. All three studies reported positive outcomes, with CCIS and incontinence episodes improving significantly. These results are encouraging, as they demonstrate the effect of SNS when all other therapies had failed and therefore improving the quality of life of patients.

Since early implementation of sacral nerve stimulation by Matzel et al. and to the best of our knowledge, it has become an effective treatment.²⁰ Overall, the findings of this crossover study confirm the positive outcomes of SNS in FI: it significantly reduced the frequency of FI episodes and CCIS, and there was a preference for ON stimulation. These results are largely consistent with the randomized multicenter crossover study published earlier by Leroi et al.¹⁶ and Volker Kahlke et al.¹⁹

However, these results should be looked at with cautious interpretation. There are many confounding factors which can affect the incontinence score and patient satisfaction which include patient age, gen-

der, pre-existing sphincter function. As a result, it is still not easy to correlate subjective and objective parameters to predict outcome for each patient and thus determine who will benefit most from current treatment modalities. From Nicholas J Kenefick early cross-over study that the beneficial clinical effect of SNS is unlikely to be due to placebo but the loss of control on fecal incontinence was seen a year later once the stimulation was removed, suggesting that repeated stimulation is required and that stimulation is a reversible neurological mechanism. However, the cases were few and further larger studies would be needed.²⁵ Furthermore J. Duelund-Jakobsen et al. (2012). study, it is known that nearly half of all patients experienced gradual loss of therapeutic effect and reported dissatisfaction would likely to occur with standard setting (14 Hz/210 μ s) during the later follow-up. The evidence for a treatment for patients experiencing loss of efficacy is limited. Altering the SNS stimulation frequency and pulse width previously to treat urinary disorders has then re-applied for treatment of fecal incontinence. Recently, it is shown that better treatment efficacy with alternative stimulation method (31 Hz/210 μ s) could then be obtained lasts at 3-month follow-up.¹⁸ Conclusions: Subsensory stimulation as low as 50% of the ST is as effective as stimulation at or above the ST.

It is also important to consider the tool for evaluation of clinical effect of SNS. Manometry is commonly used in clinical setting for patient with anal disorders. For measurement of efficacy and clinical satisfaction of SNS therapy, the role of manometry seem to be controversial. Current evidence has shown some association with changes in anorectal physiological parameters, but the results are inconsistent.^{26,27} From

Table 4. Results of changes in the number of fecal incontinence episodes per 3 weeks

Study	No. of patients	No. patients (enrolled)	Frequency of FI every 3 weeks			
			Baseline ^a	ST (100%) ^a	ST (75%) ^a	ST (50%) ^a
J. Duelund-Jakobsen et al. (2013)	27	19	33.6 \pm 31.6 ^a	0.5 \pm 1.0 ^a	1.47 \pm 2.71 ^a	2.89 \pm 6.1 ^a
	No. of patients	No. patients (enrolled)	Baseline ^b	ST (right) ^b	ST (left) ^b	ST (bilateral) ^b
J. Duelund-Jakobsen et al. (2015)	35	27	17 (3-59) ^b	2 (0-20) ^b	2 (0-42) ^b	1 (0-25) ^b

^a Mean \pm standard deviation; ^b Median (range); ST, subsensory threshold.

Nicholas J Kenefick study, anorectal physiological parameters did not change much as the stimulation parameters were altered. They suggest the possible mechanism linked to the therapeutic effect of SNS is indirect effect on the anal sphincters or pelvic floor secondary to a central neuromodulatory effect.²⁵

Although the mechanism undoubtedly involves both somatic pathways as well as the autonomic and enteric nervous systems but what has been known so far shows that SNS reduces the somatosensory evoked potential latency (SEPL) and increases the cortical peak amplitude after anal stimulation.^{28,29} In J. Duelund-Jakobsen et al. (2012) study,¹⁸ High-frequency stimulation (31 Hz/210 μ s) significantly improved the CCIS in comparison with stimulation at 14 Hz/210 μ s ($p = 0.014$).²⁸ However, frequencies of 50 Hz and above seems to be the limits to the stimulation of nerve fibres, otherwise neural damage and progressive sphincter fatigue could likely to occur.^{30,31}

The clinical individual outcomes of SNS therapy can be best assessed through scoring system. Current scoring systems including the most commonly used Cleveland clinic incontinence score (CCIS) and Fecal Incontinence Quality of Life Scale (FIQLS). For all three RCT studies, CCIS was significantly improved during the ON period but Altomare reported that when stimulation was terminated a median 28 months after implantation that only 10 of 19 (53%) patients went back to stimulation due to recurrent FI within 1 year.³² Even Maeda et al. recommended a “stimulation holiday” to restore the therapeutic effect in cases where there was a loss of efficacy, may potentially leading to an improved CCIS in the study.³³ Like Leroi et al., Volker Kahlke et al. also found the FI frequency to be significantly reduced by SNS therapy, as demonstrated by comparing the ON periods with the OFF periods.^{16,21}

J. Duelund-Jakobsen et al. (2012). revealed good agreement and improvement among the patient bowel habit diary, the CCIS and two of four subdomains of the FIQLS.¹⁸ Overall, based on current evidence in the literature that it is suggested that the significant improvement in FI should be with alternative pacemaker setting under ON mode in order to achieve clinical benefit of better FI control and CCIS.

The detailed mechanisms of SNS therapy are still

unclear. However, electrophysiological studies have previously shown improvement using measurements such as s anal resting and squeezing pressures are markedly.^{4,9}

Nevertheless, these results of all these studies raise the same problem of the choice of criteria needed to comprehensively evaluate treatment outcome both subjectively and objectively. To better assess the real impact of any treatment of FI, we recommend that future placebo-controlled protocols should include an evaluation of CCIS in combination with physiologic finding such as anal squeeze pressure.

Conclusion

The clinical benefit and improvement on quality of life can be obtained through SNS therapy during ON periods. Based on current evidence the long lasting effect of SNS therapy with high patient satisfaction comes with alternative pacemaker setting at high-frequency stimulation. Further larger studies are needed to clarify this issue.

References

1. Macmillan AK, Merrie AEH, Marshall RJ, Parry BR. The prevalence of fecal incontinence in community-dwelling adults: a systematic review of the literature. *Dis Colon Rectum* 2004;47(8):1341-9.
2. Wong WD, Congliosi SM, Spencer MP, et al. The safety and efficacy from a multicenter cohort study. *Dis Colon Rectum* 2002;45:1139-53.
3. Michot F, Costaglioli B, Leroi AM, et al. Artificial anal sphincter in severe fecal incontinence: outcome of prospective experience with 37 patients in one institution. *Ann Surg* 2003;237:52-6. of the artificial bowel sphincter for fecal incontinence: results.
4. Matzel KE, Stadelmaier U, Hohenfellner M, Gall FP. Electrical stimulation of sacral spinal nerves for treatment of faecal incontinence. *Lancet* 1995;346:1124-7.
5. Mege D, Meurette G, Vitton V, Leroi AM, Bridoux V, Zerbib P, Sielezneff I, Club N. Sacral nerve stimulation can alleviate symptoms of bowel dysfunction after colorectal resections. *Colorectal Dis* 2017;19(8):756-63.
6. Brindley GS. Treatment of urinary and faecal incontinence by surgically implanted devices. *Ciba Found Symp* 1990; 151:267-74.

7. Tanagho E, Schmidt R. Electrical stimulation in the clinical management of neurogenic bladder. *J Urol* 1988;140:1331-9.
8. Malouf AJ, Vaizey CJ, Nicholls RJ, Kamm MA. Permanent sacral nerve stimulation for fecal incontinence. *Ann Surg* 2000;232:143-8.
9. Matzel KE, Stadelmaier U, Hohenfellner M, Hohenberger W. Chronic sacral spinal nerve stimulation for fecal incontinence: long-term results with foramen and cuff electrodes. *Dis Colon Rectum* 2001;44:59-66.
10. Matzel KE, Kamm MA, Stösser M, et al. Sacral spinal nerve stimulation for faecal incontinence: multicentre study. *Lancet* 2004;363:1270-6.
11. Mellgren A, Wexner SD, Collier JA, et al.; SNS Study Group. Long-term efficacy and safety of sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum* 2011;54:1065-75.
12. Gallas S, Michot F, Faucheron JL, et al.; Club NEMO. Predictive factors for successful sacral nerve stimulation in the treatment of faecal incontinence: results of trial stimulation in 200 patients. *Colorectal Dis* 2011;13:689-96.
13. Brouwer R, Duthie G. Sacral nerve neuromodulation is effective treatment for fecal incontinence in the presence of a sphincter defect, pudendal neuropathy, or previous sphincter repair. *Dis Colon Rectum* 2010;53:273-8.
14. Wexner SD, Collier JA, Devroede G, et al. Sacral nerve stimulation for fecal incontinence: results of a 120-patient prospective multicenter study. *Ann Surg* 2010;251:441-9.
15. Hull T, Giese C, Wexner SD, et al.; SNS Study Group. Long-term durability of sacral nerve stimulation therapy for chronic fecal incontinence. *Dis Colon Rectum* 2013;56:234-45.
16. Leroi AM, Parc Y, Lehur PA, et al.; Study Group. Efficacy of sacral nerve stimulation for fecal incontinence: results of a multicenter double-blind crossover study. *Ann Surg* 2005;242:662-9.
17. Vaizey CJ, Kamm MA, Roy AJ, Nicholls RJ. Double-blind crossover study of sacral nerve stimulation for fecal incontinence. *Dis Colon Rectum* 2000;43:298-302.
18. Duelund-Jakobsen J, Dudding T, Bradshaw E, Buntzen S, Lundby L, Laurberg S, Vaizey C. Randomized double-blind crossover study of alternative stimulator settings in sacral nerve stimulation for faecal incontinence. *British Journal of Surgery* 2012;99(10):1445-52.
19. Kahlke V, Topic H, Peleikis HG, Jongen J. Sacral nerve modulation for fecal incontinence. *Dis Colon Rectum* 2015;58(2):235-40.
20. Thin NN, Horrocks EJ, Hotouras A, Palit S, Thaha MA, Chan CL, Matzel KE, Knowles CH. Systematic review of the clinical effectiveness of neuromodulation in the treatment of faecal incontinence. *Br J Surg* 2013;100(11):1430-47.
21. Altomare DF, Giuratrabocchetta S, Knowles CH, Munoz Duyos A, Robert-Yap J, Matzel KE, European SNSOSG. Long-term outcomes of sacral nerve stimulation for faecal incontinence. *Br J Surg* 2015;102(4):407-15.
22. Norton C, Thomas L, Hill J. NICE guidelines: management of faecal incontinence in adults: summary of NICE guidance. *BMJ* 2007;334:1370.
23. Duelund-Jakobsen J, Buntzen S, Lundby L, Laurberg S. Sacral nerve stimulation at subsensory threshold does not compromise treatment efficacy. *Annals of Surgery* 2013;257(2):219-23.
24. Duelund-Jakobsen J, Buntzen S, Lundby L, Sørensen M, Laurberg S. Bilateral compared with unilateral sacral nerve stimulation for faecal incontinence: results of a randomized, single-blinded crossover study. *Colorectal Disease* 2015;17(12):1085-93.
25. Kenefick NJ. Sacral nerve neuromodulation for the treatment of lower bowel motility disorders. *The Annals of the Royal College of Surgeons of England* 2006;88(7):617-23.
26. Moya P, Arroyo A, Lacueva J, Candela F, et al. Sacral nerve stimulation in the treatment of severe faecal incontinence: long-term clinical, manometric and quality of life results. *Tech Coloproctol* 2014;18(2):179-85.
27. Ratto C, Litta F, Parello A, Donisi L, De Simone V, Zaccone G. Sacral nerve stimulation in faecal incontinence associated with an anal sphincter lesion: a systematic review. *Colorectal Disease* 2012;14(6):e297-304.
28. Malaguti S, Spinelli M, Giardiello G, Lazzeri M, Van Den Hombergh U. Neurophysiological evidence may predict the outcome of sacral neuromodulation. *J Urol* 2003;170:2323-6.
29. Giani I, Novelli E, Martina S, Clerico G, Luc AR, Trompetto M, et al. The effect of sacral nerve modulation on cerebral evoked potential latency in fecal incontinence and constipation. *Ann Surg* 2011;254:90-6.
30. Agnew WF, McCreery DB, Yuen TG, Bullara LA. Evolution and resolution of stimulation-induced axonal injury in peripheral nerve. *Muscle Nerve* 1999;22:1393-402.
31. McCreery DB, Agnew WF, Yuen TG, Bullara LA. Relationship between stimulus amplitude, stimulus frequency and neural damage during electrical stimulation of sciatic nerve of cat. *Med Biol Eng Comput* 1995;33:426-9.
32. Altomare DF, Giannini I, Giuratrabocchetta S, Digennaro R. The effects of sacral nerve stimulation on continence are temporarily maintained after turning the stimulator off. *Colorectal Dis* 2013;15:e741-8.
33. Maeda Y, Lundby L, Buntzen S, Laurberg S. Suboptimal outcome following sacral nerve stimulation for faecal incontinence. *Br J Surg* 2011;98:140-7.

原著

對於骶神經刺激治療大便失禁的 五項交叉試驗的總結

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目的 骶神經刺激是大便失禁眾所周知的治療方法。有一些但不是全部標準流程患者治療大便失禁。以文獻系統性回顧的方式研究這個問題。

方法 在 Pubmed 和 Embase 數據庫中對 2018 年 12 月之前的所有相關文章進行了文獻檢索。如果是交叉隨機對照試驗，評估骶神經刺激治療對大便失禁患者的使用並評估以下至少一個端點，包括研究：大便失禁發作頻率，克利夫蘭臨床失禁評分 (CCIS) 和糞便失禁生活質量量表 (FIQLS)。對語言或學習規模沒有限制。

結果 確定了五篇隨機對照試驗論文，均為隨機交叉研究。其中包括 176 名患者和 104 名參與者。這 5 項研究的平均追蹤時間為 3 個月。初步結果表明永久性骶神經刺激治療植入後的良好結果。前三項研究的結果顯示在開啟期間大便失禁發作的頻率顯著降低。所有三項研究都報告了克利夫蘭診所尿失禁評分 (CCIS) 的陽性結果，其在開啟期間顯著改善，而非關閉時期。最佳刺激器設置是獨立個體的，但與標準設置 (14 Hz/210 μ s) 相比，高頻刺激 (31 Hz/210 μ s) 的患者滿意度增加和失禁發作減少的趨勢明顯 ($p < 0.05$)。而在低至感覺閾值的 50% 的亞感覺刺激與在感覺閾值或高於感覺閾值的刺激一樣有效。最後，雙側刺激在短期內不優於標準的單側刺激。

結論 該綜述表明，在開啟期間，骶神經刺激治療在大便失禁方面有顯著改善，患者滿意度較高，高頻刺激下失禁發作減少。

關鍵詞 骶神經刺激、大便失禁、隨機對照試驗論文、克利夫蘭臨床失禁評分、糞便失禁生活質量量表。

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