Original Article

Enhanced Recovery Protocol in Laparoscopic Colorectal Surgery: Experience of a Medical Center in Central Taiwan

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Key Words
Enhanced recovery protocol;
Fast track;
Laparoscopic colorectal surgery

Purpose. Enhanced recovery protocol has been proven early recovery in colorectal surgery. However, limited case number was reported in laparoscopic colorectal surgery. In this article, we will present our outcome of enhanced recovery protocol applied in laparoscopic colorectal surgery.
Patients and Methods. From Jun. 2013 to Nov. 2014, 536 patients who underwent elective laparoscopic colorectal surgery were enrolled and all followed the guidelines of enhanced recoveryprotocol. All the patient clinical characteristic data, surgical data, postoperative record were prospectively collected and retrospective analyzed.
Results. Total 536 patients were recruited in this study and we subdivided into three, groups: right colon (150), left colon (306), rectum (80). Mean post-operative hospital; stay: right colon was 5.7 days (3~22), left colon was 5.97 days (3~33), rectum was 7.1 days (3~26). The overall complication rate: right colon was 10.6%, left colon was 10.1%, rectum was 13.7%.
Conclusions. Our study showed enhanced recovery protocolin laparoscopic colorectal surgery was safe and feasible. The individual elements of fast track protocol will continue to evolve and further studies are still being developed.
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Previously by the time of second millennium, the average length of hospital stay after colorectal surgery was about 10~15 days. Against this background, Henrik Kehlet (Denmark) start to doubt why patients undergoing colorectal surgery fail to recover sooner and introduced the enhanced recovery protocol by minimizing perioperative stress response. He concluded the factor that prolong recovery phase afteruncomplicated colorectal surgery, included preoperative bowel preparation, persistent wound pain, gut dysfunction, prolong fasting, unnecessary drain, immobilization. Since then, he went on to introduce a clinical pathway to accelerate recovery after colorectal surgery, which included no bowel preparation, postoperative analgesia, early oral intake, early mobilization. After several decades, enhanced recovery protocol has been applied worldwide particularly in the field of colorectal surgery.[1]

The concept behindenhanced recovery protocol was to reduce complication rate, length of hospital

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stay and health care resources.[2] We can subdivideenhanced recovery protocol into three periods including pre-operative, intra-operative, and post-operative periods. The advancement of preoperative education and preparation, intraoperative modern anesthesia and laparoscopic approach, postoperative evidence-based care protocol result in early recovery and early discharge after colorectal surgery.[3-5] Enhanced recovery protocol combines these various techniques to improve surgical outcome and laparoscopic approach played a key role in the enhanced recovery protocol which reduce wound pain and fatigue, early recovery of bowel function, shorten hospital stay as compared to open colectomy.[6] According to Laparoscopy and fast-track multimodal management versus standard care (LAFA) study, the largest multicenter randomizes controlled trial thus far, reported that laparoscopic surgery was the only predictive factor associated with shorten hospital stay and reduce morbidity.[7] LAFA study also indicated that early feeding and mobilization, laparoscopic surgery were independent factor of early recovery. Furthermore, additional advantages of laparoscopic surgery included improved pulmonary function and overall quality of life postoperation.

In the future, disease-oriented case-payment will be the trend of colorectal surgery and medical cost, effectivenessare the most important. Both laparoscopic surgery and enhanced recovery protocol focus on minimizing surgical pain and perioperative stress, enhancing recovery, resulted in reimburstment of cost. Enhanced recovery protocol applied in laparoscopic colorectal surgery would reduce hospital stay 2 to 3 days. When compared with conventional care, patients who received fast track protocol resumed normal gastrointerstinal function earlier and less post operative complication. However, limited case number and there is still no agreement on a precise, standarized protocol in laparoscopic colorectal surgery.[7-11] Hence, the aim of this study was to evaluate the outcome of enhanced recovery protocol in laparoscopic colorectal surgery and present our enhanced recovery protocol, share our experience.

Materials and Methods

Patient selection

From Jun. 2013 to Nov. 2014, total 603 colorectal surgeries were performed at the Department of Colorectal Surgery, China Medical University Hospital (CMUH). After excluding emergent surgery, open surgery, transanal minimal invasive surgery (TAMIS) (Fig. 1), 536 patients underwent elective laparoscopic colorectal surgery in accordance with our enhanced recovery protocol (Table 1). We subdivided enrolled patients into three groups depending on tumor location: right colon (cecum to middle transverse colon), left colon (middle transverse colon to upper rectum), rectum (middle and lower rectum). Demographic information was collected prospectively including age, gender, body mass index (BMI), underlying disease,

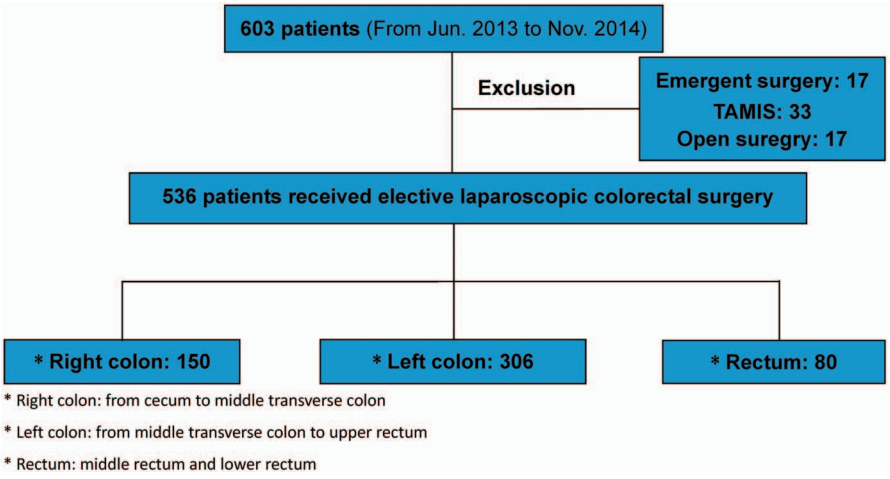

Fig. 1. Flowchart of patient selection.

Table 1. Enhanced recovery protocol of colorectal surgery in CMUH

Pre-operative period
Education
No bowel preparation
NPO 8 hours before operation
Intra-operative period
Prophylactic antibiotics
Anesthesia (no epidural cantheter)
FOLEY tube insertion
NG tube insertion was not routinelyand removed before extubation
Laparoscopic surgery all standardization
Post-operative period
Analgesics with pethidine
Try water 4 hours after operation and oral intake POD 1
Mobilization POD1
Remove foley POD1
Remove drain POD4
Discharge POD6

previous abdominal operation history, American Society of Anesthesiology (ASA) class, tumor location and histology, operation time, time to passage of flatus, postoperative hospital stay, perioperative complications and readmission within 30 days after operation. Perioperative complications were defined as those occurring within the first month of the surgical procedure.

Pre-operative period

Before surgery, patient was educated the detail of fast track protocol and early discharge by attending doctor at outpatient clinic. All of team member including attending doctor, resident, nurse practitioner, nurse followed the same enhanced recovery protocol to ensure quality control and nurse practitioner will record patient recovery course. Preoperative ante-grade bowel preparation was executed only for rectal surgery and natural orifice specimen extraction (NOSE). We used Monobasic & Dibasic Sodium Phosphate 90 mL or polyethylene glycol 2 L before surgery for bowel preparation. Patient started nothing-by-mouth at midnight. Prophylactic antibiotic (Cefmetazole 1 g) was administered thirty minutes before surgery.

Intra-operativeperiod

All laparoscopic colorectal surgeries were performed by five well-experience doctors and all procedure including trochar placement, energy usage, staple choice, anastomosis method were all standardized. NOSE for left-sided colorectal cancers was preserved for tumor size < 5 cm, no colonic obstruction, no perforation, body mass index (BMI) < 33 kg/m2. After general anesthesia, FOLEY was inserted and NG insertion only for stomach distension noted during operation. NG removed immediately after operation.

Post-operative period

After operation, a prophylactic antibiotic was administered only for intraperitoneal contamination occurred during the operation. Patients would try water soon after recovery from anesthesia, and soft diet was offered if patient tolerance. Medicine for postoperative pain controlwas used depending on the patient's request and notroutinely administered. Patient controlled analgesia usage depends on patient choice; meperidine intramuscular injectionwas used for postoperative pain relief. The urinarycatheter was removed on the first postoperative day, and encourage patient early mobilization. In our enhanced recovery protocol, scheduled discharge was post operative day 6 and discharge criteriaincluded tolerance of at least six general meals withoutnausea or vomiting, absence of abdominal distention, flatus passage, and no signs of infection or leakage.

Statistical analysis

SPSS 17.0 software was used for all statistical analyses. The ANOVA was used to compare the continuousvariables. The Pearson's chi-squared testwas usedto compare the discrete variables. $p < 0.05$ was consideredstatistically significant.

Results

There are total 536 patients were recruited from a

single institution from Jun. 2013 to Nov. 2014. All received laparoscopic colorectal surgery in accordance with enhanced recoveryprotocol. We subdivided into three groups: right colon (150), left colon (306), rectum (80). Patient demographic characteristics data was shown in Table 2. Between three groups, there is significant difference in age ($p = 0.007$) and histology ($p = 0.044$). The mean age of right colon: 65.6 (30~93), left colon: 62.02 (19~93), and rectum: 60.38 (32~85). Malignant ratio of right colon: 87.5%, left colon: 91.7%, and rectum: 97.4%.

Mean post-operative hospital stay was 5.7 (3~22) days in the right colon, 5.97 (3~33) days in the left colon, 7.1 (3~26) days in the rectum ($p = 0.018$). In the group of right colon, scheduled discharge within post-operative day (POD) 6 was 107 (75.9%), and readmission within 30 days was 5 (3%) (Table 3). In the group of left colon, scheduled discharge within POD 6 was 224 (77.2%), and readmission within 30 days was 8 (2.6%). In the group of rectum, scheduled discharge within POD 6 was 51 (65.4%), and readmission within 30 days was 2 (2.4%). The cause of delayed discharge within POD6 was shown in Table 6. The most common reason was patient insurance benefits or living in the remote districts without medical resource and complication was the second common reason.

The recovery parameters were shown in Table 4. All patients had the NG tubes removed immediately after operation and removed Foley post-operative day 1. No significant difference was found between three groups, except flatus passage ($p = 0.03$). In the group of right colon, the mean flatus passage was 1.7 (1~4) days, pain score on POD 3 was 2.4 (1~5), re-on NG

Table 2. Patient demographic characteristics

	Right colon	Left colon	Rectum	*p* value*
Patient number	150	306	80	
Male/female	75/74	171/135	47/33	0.222
Age (years), mean (range)	65.6 (30~93)	62.02 (19~93)	60.38 (32~85)	0.007
ASA*, number (%)				0.622
I	3 (1.9%)	4 (1.6%)	0	
II	87 (57.6%)	202 (65.7%)	58 (71.6%)	
III	60 (40.3%)	100 (32.5%)	20 (25.9%)	
IV	0	0	1 (1.2%)	
BMI, mean (range)	23.6 (14.6~37)	23.6 (14.6~35.6)	23.7 (15.6~35.9)	0.770
Histology				0.044
Malignant	132 (87.5%)	280 (91.7%)	78 (97.4%)	
TNM*				
Stage I, Tis	29 (21.3%)	67 (23.9%)	21 (27.2%)	
Stage II	28 (21.3%)	75 (26.7%)	29 (37.6%)	
Stage III	50 (38.1%)	75 (26.7%)	18 (24.6%)	
Stage IV	25 (19%)	63 (22.5%)	9 (11.6%)	
Benign	18 (12.5%)	26 (8.3%)	2 (2.6%)	
Polyp	15	18	0	
Diverticulosis	2	4	0	
Ulcerative colitis	0	1	1	
Others*	1	3	1	
Abdomen surgery history				0.862
Yes	40 (26.4%)	74 (24.1%)	22 (26.9%)	
No	110 (73.6%)	232 (75.9%)	59 (73.1%)	

p value * The ANOVA test was used to compare the continuousvariables and Pearson's chi-squared test was used to compare the discrete variables.

ASA * American Society of Anesthesiology score.

TNM * TNM classification system of the union for International cancer control (UICC).

Others * includingintraabdominal fistula, Cronkhite-Canada syndrome, colon inertia, rectal prolapse,solitary fibrous tumor.

was 3 (2%), re-on Foley was 3 (2%). In the group of left colon, the mean flatus passage was 1.5 (1~5) days, pain score on POD 3 was 2.3 (1~6), re-on NG was 17 (5.6%), re-on Foley was 2 (0.7%). In the group of rectum, the mean flatus passage was 1.1 (1~3) days, pain score on POD 3 was 2.2 (1~4), re-on NG was 4 (5%), re-on Foley was 3 (3.8%).

The post-operative complication was listed in Table 5. Overall complication rate of right colon was 10.6%, left colon was 10.1%, rectum was 13.2% and there was no significant difference ($p = 0.358$). Prolong ileus was the most common complication in the right colon (3.3%) and left colon (4.9%). In the group of rectum, leakage was the most common complication. There are nine patients needing reoperation including: leakage (6), bleeding (2), ischemia bowel (1) and we all tried laparoscopic approach to manage complication except ischemia bowel.

Table 3. Post-operative hospital stay

	Right colon (n = 150)	Left colon (n = 306)	Rectum (n = 80)	*p* value
Post OP hospital stay (days)				0.018
Mean (range)	5.7 (3~22)	5.97 (3~33)	7.1 (3~26)	
Discharge ≦ POD6				
Number (%)	107 (75.9%)	224 (77.2%)	51 (65.4%)	
Discharge on POD3	10 (7.1%)	24 (8.3%)	3 (3.8%)	
Discharge on POD4	33 (22.9%)	86 (29.6%)	4 (5.1%)	
Discharge on POD5	42 (29.2%)	73 (25.1%)	5 (23.1%)	
Discharge on POD6	22 (15.3%)	41 (14.1%)	26 (33.3%)	
Readmission				
Number (%)	5 (3%)	8 (2.6%)	2 (2.4%)	

Table 4. Post-OP recovery parameter

	Right colon (n = 150)	Left colon (n = 306)	Rectum (n = 80)	*p* value
Flatus passage* (POD)				0.03
Mean (range)	1.7 (1-4)	1.5 (1-5)	1.1 (1-3)	
Pain score on POD3				0.19
Mean (range)	2.4 (1~5)	2.3 (1~6)	2.2 (1~4)	
Re-on NG				0.083
Number (%)	3 (2%)	17 (5.6%)	4 (5%)	
Re-on Foley				0.231
Number (%)	3 (2%)	2 (0.7%)	3 (3.8%)	

Flatus passage * Patient who has stomy was recorded as first production from stomy.

Table 5. Post-OP complication

	Right colon (n = 150)	Left colon (n = 306)	Rectum (n = 80)	*p* value
Complication rate, n (%)	16 (10.6%)	31 (10.1%)	11 (13.7%)	0.358
Leakage	1 (0.6%)	4 (1.3%)	5 (6.2%)	
Bleeding	0	2 (0.6%)	0	
Ischemia bowel	1 (0.6%)	0	0	
Prolong ileus	5 (3.3%)	15 (4.9%)	3 (1.2%)	
Chylous ascites	3 (2%)	1 (0.3%)	0	
Wound infection	3 (2.5%)	4 (1.3%)	0	
Intra abdominal abscess	1 (0.6%)	1 (0.3%)	0	
Urine retention	2 (0.6%)	2 (0.6%)	3 (3.7%)	
Pneumonia	0	2 (0.6%)	0	

Table 6. Reason for delayed discharge > POD 6

	Right colon (n = 150)	Left colon (n = 306)	Rectum (n = 80)
Total no. of delayed discharge	43	82	29
Leakage	1	4	5
Bleeding	0	2	0
Ischemia bowel	1	0	0
Prolong ileus	5	15	3
Chylus ascites	0	1	0
Wound infection	3	3	0
Intra abdominal abscess	1	1	1
Urine retention	2	2	2
Pneumonia	0	2	0
Old age with cormobidity	4	5	2
Combine surgery*	4	13	0
Others*	22	34	16

Combine surgery * including hepatectomy, gastrectomy, cystectomy, hysterectomy.
Others * patientinsurance benefits or living in the remote districts without medical resource.

Discussion

Laparoscopic colorectal surgery has been accepted with increasing frequency worldwide due to minimal invasive injury and improved short-term outcome. Prospective randomized trials have shown that laparoscopic colorectal surgery accelerated recovery and the same long-term oncological outcome compared with open method.[4,6] However, these trials were not in accordance with enhanced recovery protocol. Compared with traditional care, enhanced recovery protocol have shown rapid recovery, reduce hospital stay and complication. In the aspect of recovery and hospital stay, laparoscopic surgery and enhanced recovery protocol have the same benefit. If both of two are combined, additionaladvantages of postoperative recoverywill be expected. Published literatures have proven applying enhanced recovery protocol in laparoscopic colorectal surgery would reduce hospital stay to 2~3 days [13-15] but case numbers were limited. In this article, 536 patients were recruited and all received laparoscopic colorectal surgery in accordance with enhanced recovery protocol.

Enrolled patientswere subdivided into right colon, left colon due to different embryology origin and rectum was classified individuallydue to complicated anatomical structure. Laparoscopic rectal resection was considered technically challenging compared to colonic resection and NygrenJpresented that enhanced recovery protocol applying in rectal surgery showed little benefit compared with colon.[5] However, enhanced recovery protocol applying in the rectum showed comparable recovery with colon in our study (Table 4). Furthermore, flatus passage in the rectum was faster than colon. But in the aspect of hospital stay, rectum was 7.1 days still longer than right colon (5.7 days), left colon (5.9 days) (p = 0.018). In the rectum, leakage was main complication that was up to 6.2% higher than colon (0.6%~1.3%) and it was also a vital cause of delayed discharge in the rectum.

The mean hospital stay in published studies were varied from 3 to 9 days (Table 7). According to these data,our patients were scheduled to be discharged on POD 6. Although some studies reported mean hospital stay within 5 days, but readmission rate was ranged from 8% to 15%, higher than our study (2.4 to 3%). There were fifteen readmission cases in our study, and ten patients due to ileus, one with intra-abdominal abscess, three had wound infection and one with uncontrolled underlying medical disease. All of these patients were treated smoothlywithout re-operation. Readmission disrupts the predicted recovery course for patient and family. It would waste more medicalcost and resource. Therefore, our surgical dischargeinterventions engage resident, nurse practitioner, case managerto improvesurveillance and communication with discharged patientsso that preventing the need for readmission.

Since enhance recovery protocol was proposed by Henrik Kehlet, many experts have published variations on the nature of optimal enhanced recovery protocol. In our protocol, we emphasized on laparoscopic approach without bowel preparation, early feeding, early removal of Foley and early ambulation. At preoperative stage, we thinkante-grade bowel preparation may lead to dehydration and electrolyte imbalance.[16] Moreover, liquid bowel content may result in anastomosis dehesience or stool spillage more frequent than solid stool.[17] However, ante-gradebowel preparation was still necessary in the surgery of mid-

Table 7. Fast track of laparoscopic colorectal surgery

Reference	Country	Design	Patient (n)	Surgery	LOS	Readmission	Complication
Chen et al., 2011 [10]	Taiwan	Prospective cohort study	80	Lap. rectal surgery	5 (3~22)	7 (9%)	11 (14%)
Stottmeier et al., 2012 [22]	Denmark	Prospective cohort study	102	Lap. rectal surgery	5 (2~42)	15 (15%)	25 (25%)
Huibers et al., 2012 [23]	Netherlands	Retrospective case control	43	Lap. rectal surgery	7 (2~83)	5 (12%)	17 (40%)
Lee et al., 2011 [24]	South Korea	RCT	46	Lap. Colon surgery	7 (6~8)	0 (0%)	6 (11%)
Vlug et al., 2011 [7]	Netherlands	RCT	193	Lap. Colon surgery	5 (4~8)	13 (7%)	125 (65%)
Wang et al., 2012 [25]	China	RCT	40	Lap. Colon surgery	5.5 (5~6)	ND	2 (5%)
Wisam et al., 2014 [26]	Israel	Prospective cohort study	71	Lap. colorectal surgery	POD 4.4	3 (4%)	6 (8.5%)

dle and low rectal patients who had protective stoma. At postoperative stage, NG tube wasunnecessary except ileus or bowel obstruction. No evidence showed NG tube was useful postoperatively and it may additionally increase patient discomfortable.[18] In our study, rate of re-on NG tube were about 2%~5%. Therefore, we think avoidance of NG tube postoperatively was safe and feasible. There are many methods reported to promote bowel motility postoperatively such as early feeding, magnesium oxide, gum chewing, and early feeding was the most important. Early feeding has been shown many advantages including promote bowel motility due to gastrocolic reflex, maintaining absorptive integrity of the bowel, maintenance of energy and protein homeostasis, decreasing insulin resistance, promote wound healing, reduce sepsis risk.[19]

Preoperative education and counseling were very important in enhanced recovery protocol. A clear explanation of hospitalization and operation course would facilitate patients compliance to the care pathway. Moreover, the success of enhance recovery protocol depends on patient active participation.[1] In Taiwan, many patients intended to live in the hospital till well recovery due toprivate insurance benefits, cheap medical resource and inherent culture. In our study, the major cause of delayed discharge within POD 6 was patient'sinsurance benefits or living in the remote districts without medical resource. Furthermore, education of colleagues is also a vital aspect for implementation of program. Several experts have stated the importance of increasing awareness and enthusiasm in all staff groups who will workwith the enhance recovery protocol.[20]

Although enhanced recovery protocol has shown comparable outcome, the individual elements that make up such programs will continue to evolve. For example, theanaesthetic protocols need to change, including clear liquid intakepreoperative, using of short acting agents (propofol), avoiding long acting opioids (morphine, fentanyl), epidural analgesia, strict fluid maintenance during operation. The evolutionof surgical technique, such as NOSE, single-port surgery evolved to reduce trauma. The outcome of NOSE surgery was better compared with traditional laparoscopic surgery.[21] However, these techniques are still being developed, randomized controlled trials comparing to traditional laparoscopic surgery within enhanced recovery protocol.

Conclusions

The enhanced recovery protocol was safe and feasiblein laparoscopic colorectal surgery. The outcomes of shorter hospital stay and faster flatus passage were acceptable and seems to have lower readmission rate. But further more studies and clinic trials are ongoing for more evidence support.

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原　著

快速恢復路徑運用於腹腔鏡大腸直腸手術

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目的　快速恢復路徑已經證實於大腸直腸手術病人可以加速恢復，但運用於腹腔鏡大腸直腸手術的文獻報告數目卻不多。這篇文章中將提出我們快速恢復路徑運用於腹腔鏡大腸直腸手術的經驗與成果。

方法　從 2013 年 6 月至 2014 年 11 月，536 位病人接受腹腔鏡大腸直腸手術以及快速恢復路徑。所有病患基本資料，手術中資料，術後併發症，住院天數前瞻性收集以及回溯性分析。

結果　全部 536 位病人接受腹腔鏡大腸直腸手術以及快速恢復路徑，並分成右結腸 (150)、左結腸 (306)、直腸 (80)。平均住院天數：右結腸 5.7 天、左結腸 5.97 天、直腸 7.1 天。併發症：右結腸 10.6%、左結腸 10.1%、直腸 13.6%。

結論　快速恢復路徑運用於腹腔鏡大腸直腸手術是安全可行的。未來快速恢復路徑必須持續的更新發展以及更多的研究證實其可行性。

關鍵詞　快速恢復路徑、腹腔鏡手術、大腸直腸切除手術。