Fast-track versus traditional perioperative care for laparoscopic colorectal surgery: a prospective randomised trial (abridged secondary publication)

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KEY MESSAGES

1. Compared with traditional perioperative care, fast-track (FT) perioperative care for laparoscopic surgery for colorectal cancer resulted in faster clinical recovery, reduced morbidity, less stress response, and better-preserved cell-mediated immunity.
2. FT perioperative care was an independent predictor of shorter total postoperative hospital stay.
3. The total direct cost was significantly lower in patients who received FT perioperative care.

Hong Kong Med J 2020;26(Suppl 8):S18-21
HHSRF project number: 08090061

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Introduction

Compared with open surgery, laparoscopic colorectal surgery is associated with better short-term clinical outcome in terms of pain, gastrointestinal recovery, and hospital stay. In a traditional perioperative care setting, the reduction in hospital stay following laparoscopic surgery is modest.[1] Laparoscopic colorectal surgery requires a long operative time and expensive disposable instruments. As such, its cost-effectiveness is a major concern for hospital administrators and policy-makers.

Fast-track (FT) perioperative care can reduce surgical stress and enhance recovery following colorectal surgery.[2] Hospital stay after open colectomy can be reduced to 2 to 3 days with the FT perioperative care. Nonetheless few studies have evaluated the impact of FT perioperative care on the clinical and immunological outcome of laparoscopic colorectal surgery.[3,4] We aimed to evaluate the clinical (hospital stay and quality of life) and immunological (systemic cytokine response and cell-mediated immune function) outcome in Hong Kong Chinese patients who underwent laparoscopic surgery for colorectal cancer and received either FT or traditional perioperative care.

Methods

Study participants

This study was conducted from December 2010 to March 2013. The study protocol was approved by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee, and registered with ClinicalTrials.gov (NCT01341366). Inclusion criteria were consecutive patients aged 18 to 80 years with American Society of Anesthesiologists grade I to III who underwent elective laparoscopic resection of colonic or upper rectal cancer. Patients were excluded if they underwent laparoscopic resection of mid or low rectal cancer, complex/combined laparoscopic procedures, or emergency surgery, had a stoma created, developed intraoperative problems that required conversion, or had known metastatic disease or a history of midline laparotomy.

Study design

Patients were randomised to receive FT or traditional perioperative care, stratified for right-sided or left-sided colorectal resection. A sealed opaque envelope (according to the computer-generated random sequence) was used to determine the appropriate programme of care. All laparoscopic surgeries were performed by experienced colorectal surgeons. Clinical outcome was assessed by an independent research assistant daily from day 0 until the day of discharge. Discharge criteria were similar for both groups, and consisted of adequate pain control, ability to tolerate solid food, ability to mobilise independently, and acceptance of discharge by the patient. Patients were telephoned daily by a designated registered nurse until review at the outpatient clinic on day 14. Patients were seen again at the outpatient clinic at 4 and 12 weeks.

Interventions

Details of the FT and traditional perioperative care are summarised in Table 1. The FT perioperative care was based on a consensus among our surgeons, anaesthetists, physiotherapists, dieticians, and nurses

TABLE 1. Comparison of the fast-track and traditional perioperative care

Phase	Fast-track perioperative care	Traditional perioperative care
Preoperative		
Colorectal clinic (surgery)	• Scheduling of surgery • Information about fast-track perioperative care, discussing discharge on day 5 if possible • Informed consent	• Scheduling of surgery • Informed consent
Preoperative clinic (anaesthesia)	• Pre-assessment for risk adjustment • Discussion focusing on fast-track anaesthetic and postoperative pain management • Explanation of pain assessment using visual analogue scale (VAS)	• Pre-assessment for risk adjustment • Explanation of intravenous patient-controlled analgesia (PCA) for postoperative pain management • Explanation of pain assessment using VAS
Preadmission counselling and guided tour on surgical ward	• Yes	• No
Admission day		
Bowel preparation	• Klean-Prep (Norgine Ltd., Middlesex, UK) x 4 L	• Klean-Prep (Norgine Ltd., Middlesex, UK) x 4 L
Diet	• Last meal 6 hours before surgery	• Last meal by midnight the day before
Preoperative carbohydrate-loaded drink	• Polycal Powder (Nutricia Advanced Medical Nutrition, UK) x 500 mL the evening before surgery	• No
Surgery day		
Pre-anaesthetic medication	• No	• No
Anaesthetic management	• Induction with fentanyl 1 μg/kg, propofol 2 mg/kg, and rocuronium 0.6 mg/kg • Anaesthesia maintained with propofol infusion 4-8 mg/kg/h and remifentanil infusion 0.05-0.2 μg/kg/min • Ventilation maintained with 40% oxygen in air • Forced body heating (Bair Hugger system and warmed intravenous fluids) • Give tramadol 1 mg/kg intravenously upon skin incision • Give parecoxib 40 mg intravenously after skin closure • Prophylactic use of ondansetron 4 mg intravenously to prevent postoperative nausea and vomiting • Intraoperative fluid restriction of crystalloid solution to 10 mL/kg and titrate with urinary output of >0.5 mL/kg/h • Intraoperative blood loss will be replaced with colloid solution	• Induction with fentanyl 1 μg/kg, propofol 2 mg/kg, and rocuronium 0.6 mg/kg • Anaesthesia maintained with sevoflurane 0.5-1.5% and oxygen 40% in nitrous oxide • Forced body heating (Bair Hugger system and warmed intravenous fluids) • Give morphine 0.1 mg/kg intravenously upon skin incision • Use of metoclopramide for postoperative nausea and vomiting according to list anaesthetist • No restriction on intraoperative fluid management
Surgical management	• Minimally invasive incisions • Infiltration of wounds with 0.5% levobupivacaine 0.2 mL/kg • Continuous wound instillation with 0.5% levobupivacaine using the ON-Q PainBuster System (I-Flow Corporation, Lake Forest, CA, USA) at 2 mL/h for 48 h • Urinary catheter • Use of abdominal drain	• Minimally invasive incisions • No infiltration of surgical wounds with local anaesthetic drugs • Urinary catheter • Use of abdominal drain
Early postoperative management	• Give incremental doses of fentanyl 10 μg intravenously if severe pain in recovery room • Add oral tramadol 50 mg plus paracetamol 1 g 3 times per day for 3 days as postoperative analgesia • Consider oral or intramuscular tramadol 50 mg for rescue pain if VAS ≥4 • First oral drink at 2 h after surgery + intravenous infusion of crystalloid solution 1.5 L/day • Sit out in chair in the evening (>2 h out of bed)	• Give incremental doses of morphine 1 mg intravenously if severe pain in recovery room • Postoperative analgesia provided by intravenous PCA morphine for 3 days (add oral tramadol 50 mg plus paracetamol 1 g 3 times per day from day 2 onwards) • 'Nil by mouth' + intravenous infusion of crystalloid solution 2 L/day • No mobilisation scheme
Day 1	• Offer soft diet • 'Extra' sugarfree gum 3 times per day • Stop intravenous fluid (leave cannula) • Remove urinary catheter • Expand mobilisation (>6 h out of bed)	• Sips of water' orally • No chewing gum • Intravenous fluid administration 2 L/day • Mobilisation according to attending surgeon
Day 2	• Offer normal diet • 'Extra' sugarfree gum 3 times per day • Remove intravenous cannula • Remove drain • Expand mobilisation (>8 h out of bed)	• Diet increases on daily basis • No chewing gum • Intravenous fluid administration is continued until adequate oral intake • Removal of urinary catheter and abdominal drain at discretion of attending surgeon • Mobilisation according to attending surgeon
Day 3	• Continue as on day 2 until discharge criteria are fulfilled	• Continue as on day 2 until discharge criteria are fulfilled

who had reviewed the relevant evidence and made appropriate adjustments to suit the local situation.[2-4]

Determination of immunological outcome

Peripheral venous blood samples were taken preoperatively and at 2 hours, 8 hours, 24 hours, 48 hours, and 5 days after surgery for measurement of systemic cytokine and cell-mediated immune responses. Interleukin-1β (IL-1β) and interleukin-6 (IL-6) were measured in triplicate by enzyme-linked immunosorbent assay. C-reactive protein (CRP) was measured by immunoturbidimetry. Lymphocyte subsets were measured using FACSCalibur flow cytometer after immunophenotyping.

Main outcome measures

The primary outcome measure was total postoperative hospital stay (including that of patients readmitted within 30 days of surgery). The secondary outcome measures were (1) immunological parameters, including cytokine and CRP levels, and lymphocyte subsets, (2) pain score on a visual analogue scale, (3) morbidity and mortality within 30 days, (4) readmission rate, (5) quality of life at 2 and 4 weeks measured by the SF-36 questionnaire, and (6) direct medical costs.

Statistical analysis and sample size estimation

Data were analysed according to the intention-to-treat principle. Confounders that might affect length of hospital stay were adjusted using multiple linear regression analysis. A two-sided P value <0.05 was considered statistically significant.

The mean hospital stay for laparoscopic resection of colonic and upper rectal cancer with traditional perioperative care in patients aged <80 years was 8 (standard deviation, 6) days at our institution. Assuming that the FT perioperative care could reduce the hospital stay to 5 days, a sample size of 64 patients in each group was needed to yield a power of 80% with a significance level of 0.05.

Results

Between December 2010 and March 2013, 157 consecutive patients were assessed for eligibility. Of these, 22 were excluded and 135 were randomised to receive FT (n=68) or traditional (n=67) perioperative care. Four patients in the FT group and three patients in the traditional group were excluded after randomisation because of conversion to laparotomy. No patients were withdrawn or dropped out. Baseline characteristics of the two groups were comparable (Table 2).

Primary outcome measure

Compared with the traditional group, the FT group had shorter median postoperative hospital stay (4 vs 5 days, P<0.001) and total postoperative hospital stay (4 vs 5.5 days, P<0.001) [Table 2]. In multiple linear regression analysis, FT perioperative care was an independent predictor of shorter total postoperative hospital stay (P<0.001), whereas presence of complications (P<0.001), right-sided colonic resection (P=0.011), and male gender (P=0.046) predicted a longer hospital stay.

Secondary outcome measures

The FT group was superior to the traditional group in all recovery parameters, including lower pain score, earlier return of gastrointestinal function, and shorter time to walk independently (Table 2). The overall 30-day complication rate also was lower in the FT than traditional group (14.1% vs 28.1%, P=0.051), as was the total direct cost (HK$96 897 vs HK$110 187, P=0.054). Quality of life at baseline was similar; all SF-36 subscales declined significantly at 2 weeks. At 12 weeks, physical functioning (P=0.002), bodily pain (P=0.018), social functioning (P=0.017), and role-emotional (P=0.033) were better in the FT than traditional group.

The preoperative level of cytokines and CRP was comparable between the two groups. IL-6 level peaked at 2 hours after surgery and was lower in the FT than traditional group (58.54 vs 74 pg/mL, P=0.05); the peak level of IL-1β and CRP was comparable between the two groups. The preoperative cell count of all the lymphocyte subsets was comparable between the two groups. After surgery, a significant depression of all the lymphocyte subsets over time was observed in both groups. Cell-mediated immune responses were less suppressed in the FT group on day 1 after surgery, as indicated by more circulating total T cells (P=0.009), helper T cells (P=0.011), and natural killer-like T cells (P=0.018).

Discussion

Compared with patients who received traditional perioperative care, those who received FT perioperative care had a lower pain score, earlier return of gastrointestinal function, lower morbidity, better preservation of quality of life, and shorter total postoperative hospital stay. FT perioperative care was an independent predictor of shorter total postoperative hospital stay after laparoscopic colorectal surgery. It improved the benefits of laparoscopic colorectal surgery and reduced the duration of hospital stay without increasing the readmission rate. The total direct cost in the FT group was reduced by about HK$13 000 per patient as a result of lower hospitalisation cost and cost of managing complications. As laparoscopic colorectal surgery has a higher direct cost than open surgery, the cost savings of the FT perioperative care may help reduce the financial burden on the hospital/healthcare system and improve the cost-effectiveness of the procedure.[1]

Patients who underwent laparoscopic colorectal surgery and received FT perioperative care

had less stress response (lower interleukin-6 peak level) and better-preserved cell-mediated immunity. This was attributed to decreased preoperative fasting, administration of carbohydrate-loaded drink preoperatively, prevention of intraoperative hypothermia, and perioperative fluid restriction. FT perioperative care can maximise the immunological benefits of laparoscopic surgery for colorectal cancer that may have implications for tumour recurrence and long-term patient survival.[5]

Our study had several limitations. The study population represented a select group of patients who underwent uncomplicated elective laparoscopic resection of colonic or upper rectal cancer. Patients with mid or low rectal cancer and patients undergoing complex or combined laparoscopic procedures were excluded. These complicated cases are more likely to have a longer recovery time and higher morbidity, and it is uncertain whether FT perioperative care would be beneficial. Both study groups were admitted to the same surgical ward and cared for by the same team of surgical and nursing staff. This might have accounted for the intergroup crossover. Although the interventions were protocol-driven, a geographically separate ward for different study groups would be desirable to minimise performance bias and protocol contamination.

Conclusion

Compared with traditional perioperative care, FT perioperative care for laparoscopic surgery for colorectal cancer resulted in faster clinical recovery, reduced morbidity, lower hospital cost, less stress response, and better-preserved cell-mediated immunity. FT perioperative care was an independent predictor of shorter total postoperative hospital stay.

Funding

This study was supported by the Health and Health Services Research Fund, Food and Health Bureau, Hong Kong SAR Government (#08090061). The full report is available from the Health and Medical Research Fund website (https://rfs1.fhb.gov.hk/index.html).

References

1. Leung KL, Kwok SP, Lam SC, et al. Laparoscopic resection of rectosigmoid carcinoma: prospective randomised trial. Lancet 2004;363:1187-92.
2. Kehlet H. Fast-track colorectal surgery. Lancet 2008;371:791-3.
3. Zhuang CL, Ye XZ, Zhang XD, Chen BC, Yu Z. Enhanced recovery after surgery programs versus traditional care for colorectal surgery: a meta-analysis of randomized controlled trials. Dis Colon Rectum 2013;56:667-78.
4. Vlug MS, Wind J, Hollmann MW, et al. Laparoscopy in combination with fast track multimodal management is the best perioperative strategy in patients undergoing colonic surgery: a randomized clinical trial (LAFA-study). Ann Surg 2011;254:868-75.
5. Ng SS, Lee JF, Yiu RY, et al. Long-term oncologic outcomes of laparoscopic versus open surgery for rectal cancer: a pooled analysis of 3 randomized controlled trials. Ann Surg 2014;259:139-47.

TABLE 2. Patient characteristics and outcome

Parameter	Fast-track perioperative care (n=64)	Traditional perioperative care (n=64)	P value
No. of males:females	40:24	39:25	0.856
Age (years)	65.3±8.7	68.2±8.4	0.060
Body mass index (kg/m^2)	22.7±3.3	23.3±3.2	0.239
Patients with comorbidities	33 (51.6)	40 (62.5)	0.211
American Society of Anesthesiologists grade			0.492
I	21	16	
II	38	40	
III	5	8	
Tumour stage			0.955
pT0	11	13	
pT1	6	6	
pT2	6	4	
pT3	35	36	
pT4	6	5	
Nodal stage			0.827
pN0	42	44	
pN1	15	15	
pN2	7	5	
Types of surgery			0.508
Right hemicolectomy	22	29	
Left hemicolectomy	7	6	
Sigmoid colectomy	18	18	
Anterior resection	17	11	
Operative time (minutes)	177.2±34.8	178.1±45.4	0.896
Blood loss (mL)	20 (0-200)	20 (0-200)	0.577
Visual analogue scale pain score			
Day 1	3.8±2.0	5.1±1.9	<0.001
Day 2	2.6±1.3	3.6±1.8	<0.001
Day 3	2.2±1.2	3.0±1.5	0.001
Time to first passing flatus (days)	2.0±0.9	2.9±1.0	<0.001
Time to first bowel motion (days)	3.2±1.3	4.4±1.5	<0.001
Time to resume normal diet (days)	2.3±1.0	4.5±4.4	<0.001
Time to walk independently (days)	2.1±0.8	3.8±2.8	<0.001
Postoperative hospital stay (days)			
Median (range)	4 (2-24)	5 (4-59)	<0.001
Mean±SD	4.7±2.9	7.8±8.3	<0.001
Readmission within 30 days of surgery	4 (6.3)	4 (6.3)	1.000
Total postoperative hospital stay (days)			
Median (range)	4 (2-24)	5.5 (4-59)	<0.001
Mean±SD	5.0±3.3	8.3±8.6	<0.001
Patients with complications	9 (14.1)	18 (28.1)	0.051
Reoperation	1 (1.6)	2 (3.1)	1.000
Operative death	0	0	
Total direct cost (HK$)	96 897±18 157	110 187±51 651	0.054

* Data are presented as mean±SD, median (range), or No. (%) of patients