Fast track in large intestine surgery – review of randomized clinical trials

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Abstract
Fast track surgery is a specific perioperative procedure. Its aim is to reduce the number of complications, to improve the comfort and satisfaction of treated patients and to shorten the time of their hospital stay. In this paper we present randomized clinical trials relating to fast track surgery including patients after colorectal resection.

Key words: surgery, colorectal resection, fast track.

Introduction
Since the end of the 1990s, there have been many reports describing a method known as fast track surgery [1]. The strategy of fast track gathers various elements of perioperative procedures. It takes into account the pathophysiology of operation injury and eliminates surgical procedures that are not justified in the perspective of evidence-based medicine. Optimal preparation of a patient for the operation connected with oral and written information about the surgical procedure and postoperative course, early feeding and rehabilitation on the day of surgery and optimal pain control make up the most important elements of pre- and post-operative procedures based on fast track surgery. Intraoperative factors include minimal-access surgery, thoracic epidural anaesthesia and non-routine use of nasogastric tubes and abdominal drains [2, 3]. The results of such a procedure are a decrease in postoperative complications, improvement of patient’s comfort and satisfaction, shortening of a patient’s hospital stay, and at the same time, a reduction of costs for the hospital [4].

A large number of publications referring to fast track strategy can be found, but evidence based on clinical studies is scarce. We have reviewed randomized clinical trials (RCT) on fast track surgery in relation to colorectal resection, because on the one hand, it seems to be documented the best, but on the other hand, cancer of the colon and rectum is one of the most common malignant cancers among people. Every year, about 940,000 new cases are noted in the world, which makes it the third most frequently occurring malignant cancer following lung cancer and breast cancer in women [5]. The basic method of treatment giving the best chance of recovery is resection. Unfortunately, it is connected with the risk of postoperative complications; severe ones include anastomotic leakage, bleeding, bowel obstruction and abdominal abscess [6].

The data were collected from the PubMed database and Cochrane Collaboration Library using key words including “fast track and colorectal surgery” and other phrases relating to the discussed strategy, such as “enhanced recovery”, “multimodal rehabilitation” and “enhanced recovery after surgery (ERAS)”.

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The analysis includes only randomized clinical trials comparing fast track in colorectal resection performed classically by laparotomy and/or by a minimally invasive method using laparoscopy.

**Fast track versus conventional care**

Five randomised clinical trials were included and analysed by comparing a fast track rehabilitation programme with traditional surgery procedure in patients after colorectal resection [7-11].

The study involved 408 patients; 205 were treated with the fast track protocol, while the remaining 203 were treated with standard surgery. All patients were operated on traditionally by laparotomy. The characteristics of the individual elements of the fast track protocol in all of the analysed RCTs are presented in Table I. Preoperative education including information about the surgical procedure and postoperative care, not employing the routine use of a nasogastric tube, early postoperative oral fluid intake, introduction of solid/semi-liquid diet, and rehabilitation on the day of surgery were constant elements of the fast track protocol in all the randomised trials. Similarly, postoperative analgesic treatment was conducted through non-steroid anti-inflammatory drugs and epidural anaesthesia, avoiding opiates.

The contents of the fast-track rehabilitation programme in nearly all the analysed trials include not using mechanical bowel preparation, fasting but with carbohydrate containing liquids 2-3 h before surgery, minimal surgical incision, and early catheter removal from the urinary bladder. As opposed to fast track surgery, the main elements of traditional management included mechanical bowel preparation before the operation, and routine use of a nasogastric tube and drains. In the postoperative period, traditional analgesia and fluid infusion were used, and oral feeding was introduced on the following days after signs of returning bowel motility were noticed.

The results of individual RCTs are presented in Table II. It is difficult to compare the results precisely since the trials applied variable protocols of fast rehabilitation programmes and each study evaluated various endpoints. The criteria for discharging a patient from hospital, the parameters for defining postoperative return of bowel motility, and the criteria for measuring postoperative pain intensification were also different. Nevertheless, a detailed analysis of the results of each trial allows us to observe common trends and conclusions.

All the trials exposed a significantly shorter hospital stay when a patient was given fast track surgery. The results of a majority of studies confirm concomitantly a good tolerance to early oral diet in the fast track group with a comparable risk of surgical complications. None of the trials showed a difference in the frequency of surgical complications including severe ones such as anastomotic leakage, bowel obstruction or infection complications. Only in one trial in the fast track group were a smaller number of general complications found, including cardiological, pulmonary and thromboembolic complications, and infections of the urinary tract. However, the frequency of surgical complications was similar.

The authors of the trials found a similar frequency of readmissions to hospital in both groups of patients within 30 days of surgery. The results of postoperative pain evaluation in individual trials were not unambiguous. Delaney et al. compared both groups with respect to postoperative pain score using a visual analogue pain scale (VAS), the McGill Pain Questionnaire (MGPD) and Short Form-36 (SF-36) and quality of life using Cleveland Global Quality of Life on the days of discharge and after 10 and 30 days [11]. They did not find any differences in any of the studied parameters. Similar results were obtained by other authors [9]. However, Anderson et al. found a significant decrease in postoperative pain at rest, on movement and on coughing in the fast track surgery group 1 day after surgery, but by day 7, they did not find any differences [10].

A few trials provided data on the postoperative function of the respiratory system including forced expiratory volume in 1s (FEV1) and forced vital capacity (FVC) and did not find any significant differences between the two groups [9, 10]. In one of the trials, an interesting evaluation of the influence of the fast track experience on the length of hospital stay was made [11]. It was found that patients from the fast track group operated on by a fast track-experienced surgeon stayed in hospital for a shorter time than patients operated on by surgeons without such experience before the initiation of the study (3.8 vs. 5 days; \( p = 0.001 \)).

Spanjersberg et al. published a systematic review comparing fast track with traditional care [12]. Four RCTs with a total of 237 patients (119 fast track vs.
**Table I.** Principles of fast track rehabilitation program in randomized clinical trials compared fast track versus conventional care after colorectal resection

| Operation                      | Wang et al. [7] | Khoo et al. [8] | Gatt et al. [9] | Anderson et al. [10] | Delaney et al. [11] |
|-------------------------------|-----------------|-----------------|-----------------|----------------------|----------------------|
| Right hemicolectomy           | n = 30          | n = 5           | n = 9           |                      |                      |
| Left hemicolectomy            | n = 18          | n = 22          | –               | n = 5                | n = 16               |
| Sigmoid colectomy             | n = 28          | n = 2           | –               |                      |                      |
| Anterior resection            | n = 30          | n = 13          | n = 10          | –                    | n = 13 (7)           |

**Day before surgery**

| Bowel preparation             | No              | Yes             | No              | Yes                   |
| Carbohydrate load            | Yes             | Yes             | Yes             |                      |
| Diet (last meal)             | Yes             | Yes             | Yes             |                      |
| Prebiotic/probiotic          | Yes (7-14 d)    | Yes (7-14 d)    | –               |                      |

**Day of surgery**

| Carbohydrate load            | 2 h             | 3 h             | 3-4 h           | 3-4 h                | –                    |
| Epidural catheter            | Yes (Th10-12)   | Yes             | Yes (Th7-L2)    | Yes (Th7-L2)         | No                   |
| Minimally invasive incision  | Yes             | Yes             | Yes             | –                    |
| Surgical drains (routine placement) | No         | –               | No              | No                   |
| Nasogastric tube             | No              | No*             | Yes**           | No*                  | Yes                  |

**Early post-operative care**

| First oral drink             | 2 h after operation | Yes             | Yes             | Yes                  |
| IV fluids infusion           | 1.5 l/d            | Yes             | Yes             |                      |
| Early mobilization           | Yes               | Yes             | Yes‡            | Yes‡                 |
| Postoperative analgesia with NSAI | Yes         | Yes             | Yes             | Yes                  |
| Avoidance of opioids        | Yes               | Yes             | Yes             |                      |

**Day 1-2 after surgery**

| Diet                          | Semi-solid food◊ | On day of surgery | On day of surgery◊ | Light diet◊ | Solid food◊ |
| Remove urinary catheter      | Yes              | Yes              | Yes              |           |           |
| Expand mobilization          | > 6 h out of bed | Yes              | Walk length of ward | Walk length of ward |                      |
| Remove epidural              | 48 h             | 48 h             | 24-36 h          | 24-36 h    | –         |
| Discharge                    | 5 d (2-41)       | 5 d (3-37)       | 5 d (4-9)        | 3 d (2-7)  | 5.4 ±2.5 d |

*d – day, h – hour, NSAI – non-steroidal anti-inflammatory medications, IV – intravenous, fat 22.00 h on the evening before surgery, *on the evening before surgery, #transverse incisions were preferred, †for gastric decompression during surgery, **were placed during surgery and removed on completion of the operation, ‡intravenous fluids were discontinued if patient was able to tolerate 200 ml water/30 min, ‡‡mobilization in the evening > 2 h out of bed, ‡sitting out of bed, ◊normal diet at day 2 after surgery, ♦if patient tolerating oral fluids, ‡‡‡2 h after rectal surgery
**Table II. Fast track versus conventional care after colorectal resection results of randomized clinical trials**

|                          | Wang et al. [7] | Khoo et al. [8] | Gatt et al. [9] | Anderson et al. [10] | Delaney et al. [11] |
|--------------------------|-----------------|-----------------|-----------------|----------------------|---------------------|
|                          | FT (n = 106)    | TRAD (n = 104)  | FT (n = 35)     | FT (n = 19)          | FT (n = 31)         |
| Overall complications    | 20              | 39              | 9               | 15                   | 7                   |
| General complications    | 10              | 16              | 9               | 15                   | 7                   |
| Cardiac                  | 2               | 5               | 0               | 4                    | 2                   |
| Pulmonary                | 3               | 8               | 2               | 0                    | 2                   |
| Thrombotic               | 1               | 3               | 2               | 0                    | 2                   |
| Urinary tract            | 2               | 5               | 5               | 2                    | 1                   |
| Other                    | 2               | 5               | 0               | 3                    | 1                   |
| Surgical complication    | 10              | 16              | 9               | 15                   | 7                   |
| Anastomotic leakage      | 4               | 2               | 1               | 3                    |                     |
| Wound infection          | 4               | 7               | 0               | 4                    | 1                   |
| Bowel obstruction        | 2               | 5               | 3               | 3                    | 1                   |
| Other                    | 3               | 4               | 1               | 2                    | 3                   |
| Mortality                | 2               | 1               | 0               | 2                    | NS                  |
| Time to tolerance of diet| 1d (1-6)        | 4d (2-9)        | 45h (20-70)     | 90h (30-170)         | 48h (35-55)         |
| Duration of IV fluids    | 35h (20-65)     | 65h (25-80)     | 26h (24-37)     | 57h (42-105)         | 35h (20-65)         |
| Readmission (< 30 d)     | 4               | 9               | 3               | 1                    | NS                  |
| Length of hospital stay  | 5.1±3.1         | 7.6±4.8         | 7.5±4.8         | 7±4.8                | 7±4.8               |

FT – fast track, TRAD – traditional care, IV – intravenous, d – day, h – hour, ‡nausea and vomiting requiring reinsertion of a nasogastric tube, §diarrhoea and vomiting, *bleeding, pelvic abscess, infected catheter, **bleeding, dehydration
118 classical procedures) were included in the analysis. A shorter stay in hospital was found in the fast track group (2.94 days; 95% CI 3.69–2.19) with similar readmission rates. The risk of complications was smaller in the fast track group (RR 0.50; 95% CI 0.35–0.72), while the risk of serious complications was similar in both groups.

In another meta-analysis, 4 RCTs and 7 non-randomised (N-RCT) trials were evaluated. There was a total of 1021 patients in this analysis, including 526 patients from a fast track group and 495 patients from a conventional care group [13]. The length of hospital stay, readmission rates, mortality and post-operative complications were analysed. A shorter length of hospital stay by an average of 2.46 days was found in the fast track group (95% CI –3.43 to –1.48). However, postoperative complications (4-47% vs. 8-75%) and mortality (0-5% vs. 0-9%) did not show any significant differences. After pooling data from all the included studies, the readmission rates were similar (0-24% vs. 0-20%). After the analysis of the data from the RCT trials, the result was similar. Subgroup analysis of N-RCTs indicated lower readmission rates in the standard care group. The necessity of nasogastric tube reinsertion after the operation did not reveal any significant difference between the groups.

Fast track after open versus laparoscopic colonic resection

Basse et al. published the first blinded randomised clinical trial comparing the procedure based on multimodal rehabilitation both in a group operated on classically and by laparoscopy [14]. The study included 60 patients who had right-sided hemicolectomy or sigmoid resection. Each group had 30 patients. The trial protocol did not differ in crucial elements significantly from the earlier presented ones. Nasogastric tubes and drains were not used routinely. Normal oral intake of fluids and solid food and mobilisation were introduced between 8 h and 24 h after surgery. Discharge from hospital was planned for the second day if oral intake was sufficient, defecation had occurred and pain with oral analgesics could be controlled. Similarly to other trials, thoracic epidural anaesthesia was applied routinely, and analgesic treatment included paracetamol and non-steroid anti-inflammatory drugs, avoiding opiates. Still, in contrast to the majority of the earlier presented trials, mechanical bowel preparation and laxative drugs were provided.

Total hospital stay and median hospital stay after surgery, postoperative complications and mortality were similar in both groups of patients. No differences were found between groups regarding the return of gastrointestinal function and early patient’s mobilisation. On the first postoperative day, patients were out of bed for 10 h increasing to 14 h from day 2 with no differences between the groups. Pain level on the day of the operation and on day 1 after the surgery was higher in the group operated on by laparoscopy. On days 2 and 30 no differences were found in pain score between the two groups. The quality of sleep was worse after laparoscopy on the first postoperative night.

In 2006, collaborative blinded RCTs (LAFA study) were begun, which were to assess the advantages of fast track surgery in comparison to laparoscopic or open surgery in a systematic manner [15]. The patients were randomised into 4 groups of patients scheduled for elective right hemicolectomy or sigmoid resection. The randomisation branches included patients operated on by the laparoscopic method or open surgery combined with fast track surgery or standard care. The trial protocol was not different from other studies apart from some small differences; the preoperative period included a rectal enema, carbohydrate drink and the last meal 6 h before the operation. The nasogastric tube was removed before extubation, no drains were used routinely, rehabilitation and oral intake of fluids and solid food were started respectively 2 h after the operation and in the evening on the same day. Analgesic treatment was based on non-steroid anti-inflammatory drugs and epidural anaesthesia. The catheter from the bladder was removed routinely after 48 h.

The total postoperative hospital stay was taken as the primary endpoint; it was defined as the postoperative hospital stay plus the additional hospitalisation, if a patient was readmitted within 30 days of surgery. As secondary endpoints, the following were assumed: quality of life 2 and 4 weeks after the operation, hospitalisation costs, complications and morbidity within 30 days after the surgery, and readmission rates. Eventually, the analysis included 100 patients in the laparoscopy/fast track group, 93 patients in the open/fast track group, 109 patients in the laparoscopy/standard care groups and 98 pa-
patients in the open/standard care group [16]. All patients were operated on due to colon cancer. Participating laparoscopic surgeons were required to have performed a minimum of 20 laparoscopic colectomies; however, no quality requirements were established for open surgery. The trial was blinded for the doctors, patients and nurses by placing large dressings covering the abdomen after surgery. The operating surgeons did not take care of a patient in the postoperative ward.

A significant decrease in the total hospital stay and postoperative hospital stay was found in the laparoscopy fast track group in comparison to the other three randomised groups. Patients who had had laparotomies followed by standard care had a significantly longer postoperative hospital stay and the total hospital stay in relation to the other three groups. The total hospital stay and postoperative hospital stay did not differ only between patients treated with the open/fast track procedure and patients treated with laparoscopy/standard care. In the linear regression analysis, only laparoscopy was an independent factor which influenced the total hospital stay (0.79; 95% CI: 0.69-0.91, \( p = 0.001 \)). However, a significant influence on the shortening of postoperative hospital stay both for laparoscopy (0.80; 95% CI: 0.70-0.91, \( p = 0.001 \)) and for fast track surgery (0.86; 95% CI: 0.76-0.98, \( p = 0.025 \)) was shown. No differences between groups were found in relation to the secondary endpoints. Both rates of anastomosis leakage, mechanical ileus requiring reoperation, abdominal wall dehiscence and infectious complications, were similar in each group. The results referring to postoperative pain assessment, life quality and return of gastrointestinal function or diet tolerance were also alike.

Conclusions

Although we have access to a few RCTs on fast track surgery, it is difficult to prove, in an unambiguous manner, the advantage of one of the methods of colonic resection, or in particular rectal resection. It seems that relying on the presented RCT results, a conclusion can be drawn that using the fast track method in patients with colonic resection shortens the length of hospital stay.

It is necessary to continue further reliable studies based on a greater number of patients. This would identify unambiguously the possible advantages of using fast track surgery. In 2010, the protocol of collaborative study for randomising patients into three groups was presented (TAPAS study) [17]. The patients were treated with conventional open surgery as the control method versus patients treated with open surgery with ERAS and laparoscopic surgery with ERAS as the alternative exposure. It seems that the results of this study may answer some questions and help dissipate some existing controversies.

References

1. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth 1997; 78: 606-17.
2. Wilmore D, Kehlet H. Management of patients in fast track surgery. BMJ 2001; 322: 473-6.
3. Kehlet H. Fast-track colorectal surgery. Lancet 2008; 371: 791-3.
4. Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. Ann Surg 2008; 248: 189-98.
5. http://www.who.int/mediacentre/news/releases/2003/pr27/en/.
6. Bokey EL, Chapuis PH, fung C, et al. Postoperative morbidity and mortality following resection of the colon and rectum for cancer. Dis Colon Rectum 1995; 38: 480-6.
7. Wang G, Jiang ZW, Xu J, et al. Fast-track rehabilitation program vs conventional care after colorectal resection: a randomized clinical trial. World J Gastroenterol 2011; 17: 671-6.
8. Kho CK, Vickery CJ, Forsyth N, et al. A prospective randomized controlled trial of multimodal perioperative management protocol in patients undergoing elective colorectal resection for cancer. Ann Surg 2007; 245: 867-72.
9. Gatt M, Anderson AD, Reddy BS, et al. Randomized clinical trial of multimodal optimization of surgical care in patients undergoing major colorectal resection. Br J Surg 2005; 92: 1354-62.
10. Anderson AD, McNaught CE, MacFie J, et al. Randomized clinical trial of multimodal optimization and standard perioperative surgical care. Br J Surg 2003; 90: 1497-504.
11. Delaney CP, Zutshi M, Senagore AJ, et al. Prospective, randomized, controlled trial between a pathway of controlled rehabilitation with early ambulation and diet and traditional postoperative care after laparotomy and intestinal resection. Dis Colon Rectum 2003; 46: 851-9.
12. Spanjersberg WR, Reurings J, Keus F, et al. Fast track surgery versus conventional recovery strategies for colorectal surgery. Cochrane Database Syst Rev 2011; 16: CD007635.
13. Gouvas N, Tan E, Windsor A, et al. Fast-track vs standard care in colorectal surgery: a meta-analysis update. Int J Colorectal Dis 2009; 24: 1119-31.
14. Basse L, Jakobsen DH, Bardram L, et al. Functional recovery after open versus laparoscopic colonic resection: a randomized, blinded study. Ann Surg 2005; 241: 416-23.
15. Wind J, Hofland J, Preckel B, et al. Perioperative strategy in colonic surgery: LAParoscopy and/or Fast track multimodal management versus standard care (LFA trial). BMC Surg 2006; 6: 16.
16. 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.

17. Reurings JC, Spanjersberg WR, Oostvogel HJ, et al. A prospective cohort study to investigate cost-minimisation, of traditional open, open fast track recovery and laparoscopic fast track multimodal management, for surgical patients with colon carcinomas (TAPAS study). BMC Surg 2010; 10: 18.

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