

# Perioperative Protocols in Colorectal Surgery

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## Abstract

The reduction in health-care expenditures and more efficient use of medical resources are now overriding health policy priorities with the two-pronged goal of improving patient outcomes while decreasing overall cost. Current reports show colorectal surgery accounting for 25% of all operative complications and an average length of stay of 8 to 12 days for a standard elective colon resection. To combat this, Kehlet and colleagues introduced a concept of enhanced recovery after surgery (ERAS) or fast-track pathways, with the goal of using current evidence and multimodal therapies to decrease surgical stress, enhance postoperative recovery, and reduce length of stay. The benefits, safety, and cost-effectiveness of fast-track protocols are validated in multiple randomized controlled trials. In this review, the authors focus on the evidence regarding fast-track pathways, use of minimally invasive surgery and its role in fast-track pathways, newer perioperative interventions, and future directions.

## Keywords

- ▶ colorectal surgery
- ▶ perioperative protocols
- ▶ fast-track surgery
- ▶ enhanced recovery after surgery
- ▶ ERAS

**Objectives:** On completion of this article, the reader should be able to recognize that fast-track protocols are safe and cost-effective, while improving overall patient outcomes by reducing the surgical stress response; summarize the components of fast-track surgery by each perioperative phase; understand the role of minimally invasive surgery in colon and rectal resections and perioperative adjuncts; and outline future directions for fast-track surgery.

In 2010, health-care expenditures in the United States neared \$2.6 trillion, 10 times the amount spent in 1980.<sup>1</sup> Current projections show national health expenditures continuing to increase and account for 20% of the gross domestic product by 2020.<sup>2</sup> The reduction in health-care expenditures and more efficient use of medical resources is now an overriding health policy priority with the two-pronged goal of improving patient outcomes while decreasing overall cost. This is especially relevant in the field of colorectal surgery because of a disproportionately higher complication rate and longer length of stay when compared with other operative procedures. Current reports show colorectal surgery accounting for 25% of all operative complications and an average length of stay of 8 to 12 days for a standard elective colon resection.<sup>3–6</sup>

During the last several decades, there has been growing recognition that surgical stress caused by major surgery

results in derangements in organ function and subsequently increases postoperative morbidity. To combat this, Kehlet introduced a concept of enhanced recovery after surgery (ERAS) or fast-track pathways, with the goal of using current evidence and multimodal therapies to reduce surgical stress and enhance postoperative recovery. This was achieved by asking the simple question: Why is the patient in the hospital today?<sup>7</sup> The pathway elements are perioperative care interventions that focus on anesthesia, analgesia, reduction of surgical stress (both endocrine-metabolic and inflammatory responses), goal-directed fluid therapy, the prevention of nausea and ileus (return of bowel function), thromboembolic prophylaxis, minimally invasive techniques, nutrition, and early mobilization.<sup>8</sup>

The benefits and safety of fast-track protocols (FTPs) are validated in multiple randomized controlled trials.<sup>9</sup> Patients in these studies had faster return of bowel function, shorter length of hospitalization, and decreased complication rates. These findings were confirmed by several meta-analyses and a recent *Cochrane Review*.<sup>10–13</sup> The most recent meta-analysis included 7 randomized control trials with 852 patients. Lv et al found patients randomized to FTP care had a significantly decreased length of stay (mean difference: –1.88; 95% confidence interval [CI], –2.91 to 0.86,  $p = 0.0003$ ) and overall rate of complications (relative risk [RR] = 0.69; 95% CI, 0.51–0.93),

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$p = 0.01$ ) without differences in mortality (RR = 1.02; 95% CI = 0.40–2.57,  $p = 0.97$ ).<sup>13</sup> Initial reports demonstrated higher readmission rates in two small studies (likely secondary to the earlier discharge); however, in several subsequent meta-analyses, there was no significant difference in readmission rates between conventional care and FTP patients.<sup>10–15</sup>

Regarding concerns of higher cost, multiple studies have found FTPs to be cost-efficient, even including those that use laparoscopic surgery. Laparoscopic surgery is more expensive than open surgery secondary to disposable instruments, additional operative time, and mastery of the learning curve.<sup>16–18</sup> However, overall costs for laparoscopy are offset by reduction in length of stay, inpatient resources, and decreased complications. Delaney and colleagues reported implementation of an FTP for minimally invasive surgery at a single institution that required no additional personnel or expense.<sup>19</sup> A cost analysis in New Zealand found an initial implementation cost of \$102,000 was offset by a reduction in postoperative resource utilization and an overall cost savings of \$6,900 per patient.<sup>20</sup>

This review focuses on the evidence regarding fast-track pathways, use of minimally invasive surgery and its role in fast-track pathways, newer perioperative interventions, and future directions. Some brief overviews of the individual components are reviewed here with more detailed evidence regarding each component found elsewhere within this volume.

## Implementing an ERAS Pathway

Fast-track surgery is a multimodal effort to improve patient outcomes and decrease cost of care. As such, implementation of fast-track surgery pathway requires a multimodal approach involving the entire patient-care team. A fast-track surgery team includes a team leader, anesthesiologists, nurses, and ancillary staff such as physical therapists, enterostomal therapists, and social workers—all trained in fast-track surgery principles.<sup>21</sup>

Despite substantial evidence in the literature on the benefit and cost savings of fast-track surgery, implementation of a FTP is challenging. Several series have shown that the transition from concept to wide clinical practice is delayed.<sup>19,22–25</sup> In 2010, a Web-based survey of 407 general and colorectal surgeons found that only 30% of the surgeons practiced in hospitals that had implemented an FTP.<sup>26</sup> Internal barriers include lack of awareness of current evidence-based literature regarding benefits of fast-track surgery, disagreement with current findings, or belief that a particular hospital or institution cannot support fast-track surgery protocols. External barriers include a lack of support from staff (hospital administration, nurses, and physicians), inability to collect and maintain outcome data, lack of expertise in FTPs, financial concerns regarding cost of implementation and maintenance of FTP, and insufficient number of support staff.<sup>8,27</sup> The key to overcome many of these barriers is having the senior clinical and administrative leadership buy-in to fast-track surgery and the protocols required to make it

successful.<sup>19</sup> In addition, acceptance by the patient and his or her support system is mandatory. Education and communication of each component of fast-track pathway begins at the preoperative visit and is performed in verbal and written communications in simple, plain language. As the patient enters different phases of fast-track pathway, goals such as early ambulation, oral intake, pain control, and other discharge criteria are reiterated by all members of the team. A successful FTP hinges on patient and provider compliance, with the postoperative phase being the most critical in decreasing length of stay.<sup>28</sup>

## Components of Fast-Track Protocol

### The Preoperative Phase

FTP interventions begin with proper patient selection involving a thorough history and physical examination with all organ systems carefully reviewed to determine whether a patient requires preoperative optimization. Patients with chronic obstructive pulmonary disease, coronary artery disease, and diabetes mellitus may require additional workup and treatment before proceeding with surgery.<sup>29</sup> Ideal patients for the FTP are healthy individuals who have an American Society of Anesthesiologist (ASA) score of 1 or 2, whereas typically only a select group of patients with ASA score of 3 are optimal candidates.<sup>30</sup> Commonly reported contraindications for FTP include malnourishment (greater than 10% weight loss), immobility or minimally immobile, active alcohol abuse (more than 5 drinks per day) or dependence, poorly controlled psychiatric disorders or lack of social support, and inability to follow-up for postoperative visits or complications.<sup>29,30</sup> Patients with active alcohol abuse or dependence should be abstinent at least 4 weeks prior to surgery to decrease postoperative morbidity.<sup>31,32</sup> Active tobacco abusers are strongly encouraged to quit at least 4 weeks prior to surgery to prevent respiratory complications, although an optimal cessation period to decrease immune response and improve wound healing has yet to be determined.<sup>33–35</sup> The type of procedure being performed should also be a factor in whether FTP is utilized. Emergent procedures for ischemia, obstruction, or perforation and difficult procedures that require extensive dissection or lysis of adhesions are likely best managed by the standard postoperative protocol.<sup>30</sup> The planned surgical procedure and FTP including risks and benefits are discussed at this time with appropriate FTP patients.<sup>30</sup>

Perioperative  $\beta$ -blockade has been extensively studied in standard care perioperative protocols. Current recommendations are to continue  $\beta$ -blockade in patients with known coronary artery disease already on this therapy or those with preoperative cardiac ischemia or cardiac symptoms scheduled to undergo high-risk surgery. When the decision is made to initiate  $\beta$ -blockade therapy, it is started several weeks prior to surgery and titrated to “appropriate and individual” heart rate and blood pressure. Patients who continue or are placed on  $\beta$ -blockade therapy require close monitoring for bradycardiac or hypotensive episodes in the postoperative period.<sup>36,37</sup>

Preoperative mechanical bowel preparation (MBP) was historically considered standard procedure on the basis of the belief that it reduced infection rates and anastomotic dehiscence by decreasing fecal and bacterial load. A recent *Cochrane Review* examined patients undergoing elective colon or rectal surgeries and found no evidence of clinical benefit in prevention of anastomotic leaks or wound infections. In elective extraperitoneal rectal surgery with restoration of continuity and patients undergoing laparoscopic resection, the authors concluded that further research is required.<sup>38</sup> Recent guidelines from the Society of Alimentary Gastrointestinal Endoscopic Surgeons recommend MBP in laparoscopic surgeries to improve bowel manipulation and prepare for intraoperative colonoscopy if anastomotic visualization or lesion localization is required. In lower rectal resections or rectal resections with planned proximal diversion after resection and anastomosis, MBP is also recommended.<sup>39,40</sup> Currently, there are no studies that specifically address MBP in an FTP.

## The Intraoperative Phase

### The Pathophysiology of Surgical Stress

The surgical stress response is thought to be a conserved cellular defense mechanism occurring as a result of surgical trauma.<sup>41,42</sup> This causes changes in neural, endocrine, and metabolic systems with a shift toward catabolism, activation of sympathetic nervous system, and release of catecholamines. When surgical injury is induced, afferent neuronal impulses are stimulated at the site of injury and travel up sensory nerve roots through the dorsal horn of the spinal cord to the medulla and hypothalamus. There is a subsequent release of hypothalamic stimulating hormones and increased secretion of pituitary hormones, adrenocorticotropic hormone, antidiuretic hormone, and growth hormones.<sup>43</sup> Increased secretion of these hormones shifts the body into a hyperdynamic and catabolic state. This results in increased oxygen and cardiac demand, decreased pulmonary function, pain, gastrointestinal (GI) side effects such as postoperative nausea and vomiting (PONV) and ileus, derangements of coagulation favoring a prothrombotic state, and immunosuppression.<sup>7</sup> Tissue injury also causes activation of the inflammatory response with local and systemic effects. This is primarily mediated by cytokines, with an imbalance of proinflammatory (interleukin- [IL-] 1, IL-6, and tumor necrosis factor- $\alpha$ ) and anti-inflammatory cytokines, with the magnitude of the stress response related to the degree of surgical trauma.<sup>7,44,45</sup> Proinflammatory cytokines also activate the hypothalamus–pituitary–adrenal axis.<sup>44</sup>

The overall goal of intraoperative components in fast-track surgery is attenuation of surgical stress response. This is achieved either through blockade of inflammatory or endocrine–metabolic responses. Standard intraoperative techniques to minimize or block these responses include prevention of hypothermia, appropriate antibiotic prophylaxis, and avoidance of blood transfusions. FTP interventions also include neuraxial blockade and minimally invasive surgery.

### Neuraxial Blockade and Preemptive Analgesia

Neuraxial blockade is an anesthetic technique providing optimal pain control by delivering local and opioid analgesia directly to the dorsal horn of the spinal cord and decreasing surgical stress response by blocking afferent neural impulses from the site of surgical injury to the hypothalamus and anterior pituitary gland.<sup>45,46</sup> Epidural catheters have been shown to be superior to intravenous opioids in postoperative pain control in both open and laparoscopic surgery.<sup>47</sup> There is also benefit shown in reduction of postoperative ileus (POI).<sup>48</sup> Yet, in the FTP setting, some studies did not find a benefit to use epidural anesthesia.

Other techniques for preemptive analgesia include systemic lidocaine or transabdominal peritoneal block. Systemic lidocaine is generally administered intravenously with bolus followed by continuous infusion to attenuate surgical stress response and prevention of POI. A double-blind, randomized, placebo controlled trial found systemic lidocaine infusions significantly decreased time to GI tract recovery (8 hours earlier than control,  $p < 0.05$ ) and length of stay (7 days in lidocaine group versus 8 days in control group,  $p = 0.004$ ) and attenuated elevated plasma levels of inflammatory cytokines.<sup>49</sup>

The transversus abdominis plane (TAP) block was first reported by Rafi in 2001 and has since been modified several times.<sup>50</sup> Current technique involves infusion of local anesthetics into the neurovascular plane between the transversus abdominis muscle and the internal oblique muscle via the lumbar triangle of Petit. This regional anesthetic technique is capable of blocking the lower intercostals (T7–11), iliohypogastrics, and ilioinguinal nerves. A prospective randomized trial validated its ability to decrease postoperative opioid requirements by 70% in 34 patients undergoing open elective colorectal surgeries.<sup>51</sup> Although TAP blocks hold much promise in reduction of postoperative pain, opioid usage, and POI, more prospective randomized trials are needed to validate the above studies' findings.

### Minimally Invasive Surgery

Laparoscopy in colorectal surgery improves postoperative outcomes when compared with an open approach, largely through decreased pulmonary complications, smaller incisions resulting in decreased pain and opioid use, reduction in POI, and overall decreased average length of stay by 2 to 3 days compared with conventional length of stay.<sup>16,52,53</sup> Recent *Cochrane Reviews* confirmed short-term benefits of laparoscopic colorectal surgery and long-term outcomes of laparoscopic oncological resections.<sup>54,55</sup> Despite these findings, there is a slower rate of integration within the field of colorectal surgery, with only a third of all elective colectomies in the United States performed laparoscopically.

With introduction of FTPs into colorectal surgery, there is increasing interest in further optimizing reduction of surgical stress, and its negative effects, by adopting minimally invasive techniques. Single-center studies demonstrate a shorter length of stay (3.7–4.1 d) with no increase in readmission or complication rates.<sup>56–58</sup> Poon et al found decreased rate of POI when evaluating colorectal cancer patients undergoing

laparoscopic colectomy with FTP, but did not find a statistically significant difference in length of stay, complication, or readmission rates.<sup>59</sup>

There are also conflicting findings about cost-effectiveness. An English study reported a significant reduction in length of stay compared with open procedures (5.2 vs. 7.4 d), but higher upfront operative costs (\$4,016 vs. \$2,781), which were offset by decreased length of stay, readmission rates, and follow-up costs; the laparoscopic/FTP group actually saved \$517 (\$9,405 vs. \$9,922).<sup>60</sup> The traditional open, open fast-track recovery and laparoscopic fast-track multimodal management (TAPAS) study is an ongoing prospective cohort study evaluating cost-effectiveness of patients undergoing resection for colon cancer using laparoscopic techniques and FTPs in three treatment arms (open surgery with standard treatment, open surgery with fast-track treatment, and laparoscopic surgery with fast-track treatment). Primary outcomes are direct medical costs and indirect nonmedical costs to direct the future investment of minimally invasive techniques, FTPs, or a combination of both.<sup>61</sup>

To determine what the optimal combination of perioperative care is, several multicenter trials have been undertaken. The laparoscopy and/or fast-track multimodal management versus standard care (Lafa) study randomized patients with colon cancer to four different arms: laparoscopic colectomy with fast-track care, laparoscopic colectomy with standard care, open colectomy with fast-track care, or open colectomy with standard care. The shortest length of stay occurred in the laparoscopic/FTP group, with laparoscopy the only independent predictive factor to reduce length of stay and morbidity after regression analysis.<sup>62</sup> Further multivariate and univariate analysis of baseline characteristics and fast-track elements demonstrated early enteral feeding, early mobilization, laparoscopic surgery, and female sex as independent determinants of early recovery.<sup>63</sup> The enhanced recovery open versus laparoscopic (EnROL) trial is an ongoing multicenter, randomized control trial that stratifies patients to open or laparoscopic colorectal cancer surgery with both groups receiving fast-track care. This trial seeks to determine whether laparoscopic surgery improves outcomes compared with open surgery, even when fast-track care is used. This trial differs from the Lafa study by including patients undergoing resection for rectal carcinoma and excluding benign colorectal disease to capture a sicker, older patient population who likely have a higher complication rate and thus highlight potential benefits of laparoscopy and fast-track care.<sup>64</sup>

The use of minimally invasive surgery has also been explored in rectal surgery for both benign and malignant disease.<sup>65</sup> The most recent recommendations published by the ERAS Society strongly recommend laparoscopy in an FTP for resection of benign disease in the hands of an experienced surgeon, but not for malignant disease unless in the setting of a trial until a final consensus is reported from ongoing trials.<sup>66</sup>

Minimally invasive surgery is another fast-track surgery technique to decrease the surgical stress response and improve patient outcomes. Although more costly upfront, this is

offset by decreased length of stay, inpatient resources, and postoperative morbidity. There are multiple studies to support its use in colonic resections; however, in rectal resections current evidence is limited at this time.

## The Postoperative Phase

### Recovery of Gastrointestinal Function

POI is a dreaded, but common complication after major abdominal surgery. POI is defined as a “temporary impairment of GI function” and characterized by “bowel distension and vomiting and delay in oral feeding and increased postoperative pain.”<sup>52</sup> The exact etiology of POI is unknown, but believed to be multifactorial with activation of sympathetic reflexes at spinal and local levels and the inflammatory response. Open surgery and increased bowel manipulation may contribute to POI. Laparoscopy, as part of the FTP, is believed to reduce surgical trauma and the inflammatory response, thus avoiding the development of POI; however, a *Cochrane Review* found laparoscopy can reduce but not prevent POI.<sup>55</sup> Cost of POI management is staggering with higher mean costs and length of stay with an overall cost in the United States ranging from \$750 million to \$1.46 billion dollars.<sup>67-70</sup> FTPs attempt to lower incidence of POI by employing multimodal therapies. Current protocols include minimally invasive surgery, thoracic epidural analgesia, avoidance of routine nasogastric intubation, and early enteral feeding.

### Judicious Pain Management

The postoperative phase is the most critical phase in increasing patient compliance and decreasing length of stay. To that end, judicious and effective postoperative pain management is crucial. Systemic opioids are a traditional part of pain management, with excellent results seen with patient-controlled analgesia use; however, they are not without their side effects including worsening of POI. The use of continuous epidural analgesia, lidocaine infusions, and TAP blocks may represent methods to deliver effective pain control and attenuate the surgical stress response and should be utilized in fast-track surgery protocols.

Additional options for multimodality postoperative pain management are discussed in the last article in this issue of *Clinics in Colon and Rectal Surgery*. These include regional, local infiltration (liposomal bupivacaine), and nonopioid systemic analgesia (intravenous acetaminophen and nonsteroidal anti-inflammatory drugs).<sup>71</sup>

## Future Directions

Since its inception in the mid-1990s, FTP continues to undergo refinement in an effort to improve patient outcomes. Preoperative risk assessment is a cornerstone of all successful surgical interventions. The tools and matrices that allow for careful assessment and further optimization are based on conventional surgical protocols. As older and sicker patients undergo surgery, further studies of these patients within an FTP are needed to reassess perioperative risk.<sup>72</sup>

**Table 1** Laparoscopic colectomy with fast-track protocol

Author	Year	Total number of patients	No. of laparoscopic with FTP patients	Mean length of stay (days)	Complication rate (%)	Readmission rate (%)
Bardem et al <sup>73</sup>	2000	50	50	2.5	0.25	0.05
Basse et al <sup>74</sup>	2005	60	30	3.8	0.26	0.2
King et al <sup>60</sup>	2006	58	41	5.2	0.15	0.05
Delaney et al <sup>53</sup>	2008	118	118	3.7 ± 3.7	20.3	8.5
Reurings et al (TAPAs Trial) <sup>61</sup>	2010	120	40 <sup>a</sup>	b	b	b
Vlug et al (LAFA Trial) <sup>62</sup>	2011	427	100	5 (4–8) <sup>c</sup>	34 <sup>d</sup>	6 <sup>d</sup>
Poon et al <sup>59</sup>	2011	180	96	4 (2–23) <sup>c</sup>	12.5 <sup>d</sup>	5 <sup>d</sup>
Delaney et al <sup>57</sup>	2012	1000	1000	4.1 ± 3.2	20	6
Kennedy et al (EnROL Trial) <sup>64</sup>	2012	202	133 <sup>a</sup>	b	b	b

<sup>a</sup>Planned sample size.

<sup>b</sup>Ongoing trial.

<sup>c</sup>Median length of stay.

<sup>d</sup>Not significant,  $p > 0.05$ .

The overall reduction in surgical stress is a priority in FTP. Attenuation of this response is an active area of research. Research into the efficacy of laparoscopy in fully implemented FTPs is ongoing with the EnROL trial and results are expected in the next year (→ **Table 1**).<sup>64</sup> Natural orifice transluminal endoscopic surgery and single-incision laparoscopic surgery are the latest techniques in minimally invasive surgery, but their implementation and benefit in FTP has yet to be investigated.<sup>72</sup>

## Conclusion

Fast-track surgery uses current evidence and multimodal therapies to reduce surgical stress and enhance postoperative recovery by asking the simple question: Why is the patient in the hospital today?<sup>7</sup> Whereas FTPs may encompass different individual components, each with varying reported degrees of success, their overall usefulness is likely a reflection of the entire protocol. What seems clear is that FTPs are safe and cost-effective, and result in a reduction in both length of stay and postoperative morbidity and mortality. A successful FTP is a multidisciplinary endeavor that requires support from all members of the team, including the management of patients' expectations. Although full implementation of all components continues to be a challenge, it is important to understand the evidence behind their success. Many programs continue to exclude proven evidence-based components such as proper patient information, utilization of neuraxial anesthesia, nonopioid analgesia, or early enteral feeding.<sup>72</sup> These tools are proven to improve postoperative mobility and decrease risk of POI. Although gains in the reduction of surgical stress, patient outcome, and cost have been made, continuing reassessment and research is needed to further refine and improve upon the components of the fast-track surgery protocol.

## Disclaimers

The views expressed are those of the author(s) and do not reflect the official policy of the Department of the Army, the Department of Defense, or the US Government.

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