

COMMENTARY

Impact of Enhanced Recovery Program on Colorectal Cancer Surgery

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Abstract

Surgical outcomes of colorectal cancer treatment depend not only on good surgery and tumor biology but also on an optimal perioperative care. The enhanced recovery program (ERP) – a multidisciplinary and multimodal approach, or so called ‘fast-track surgery’ – has been designed to minimize perioperative and intraoperative stress responses, and to support the recovery of organ function aiming to help patients getting better sooner after surgery. Compared with conventional postoperative care, the enhanced recovery program results in quicker patient recovery, shorter length of hospital stay, faster recovery of gastrointestinal function, and a lower incidence of postoperative complications. Although not firmly established as yet, the enhanced recovery program after surgery could be of oncological benefit in colorectal cancer patients because it can enhance recovery, maintain integrity of the postoperative immune system, increase feasibility of postoperative chemotherapy, and shorten the time interval from surgery to chemotherapy. This commentary summarizes short-term outcomes and potential long-term benefits of enhanced recovery programs in the treatment of colorectal cancer.

Keywords: Enhanced recovery program - enhanced recovery after surgery - colon cancer - rectal cancer - survival

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Introduction

Surgical outcomes of colorectal cancer treatment depend not only on good surgery and tumor biology, but also on an optimal perioperative care. Using multimodal strategies and multidisciplinary team approach, an enhanced recovery program (ERP), or known as an enhanced recovery after surgery (ERAS) protocol or a fast-track surgery, has been designed to minimize perioperative and intraoperative stress responses, and to support the recovery of organ function aiming to help patients getting better sooner after surgery. Of note, with a conventional care, patients undergoing an operation for colorectal cancer (with or without adjuvant chemotherapy) could require 3-6 months to revert to their baseline for functional capacity and health-related quality of life (Hung et al., 2013).

Components of an Enhanced Recovery Program

In general, an ERP has 3 major elements; preoperative management, intraoperative treatment, and postoperative care (Gustafsson et al., 2013; Nygren et al., 2013): *i*) Preoperative management aims to optimize preoperative condition of the patients including detailed preadmission counseling, avoidance of prolonged fasting, appropriate nutrition support, carbohydrate loading, breathing exercise, a selective use of mechanical bowel preparation,

adequate hydration, administration of short-acting pre-anesthetic medication, appropriate intravenous antibiotic prophylaxis, and proper use of deep vein thrombosis prophylaxis: *ii*) Intraoperative treatment consists of preemptive analgesia, epidural analgesia, non-midline incision if appropriate (Lohsiriwat et al., 2009), minimally invasive surgery if possible, goal-directed intravenous fluid therapy, active warming, no nasogastric intubation, and avoidance of unnecessary drain and stoma (Lohsiriwat et al., 2008); *iii*) Postoperative care comprises early feeding and appropriate nutrition support, early mobilization, preventive analgesia with the preferential use of non-opioid analgesia, prophylaxis of postoperative nausea vomiting, prevention of postoperative ileus, scheduled removal of urethral catheter, regular audits and outcome measures.

In general, patients would be early discharged from the hospital if they are clinically stable, have good recovery of gastrointestinal function and no fever, and are capable of having self care and mobilization with adequate pain control using oral analgesia. Of note, it was evident that perioperative comprehensive supportive care interventions, including health education, psychological support and stress management, were associated with a better general health status and a higher patient's satisfaction as well as a shorter hospital stay in patients with gastrointestinal malignancy (Zhang et al., 2013).

For elective colorectal surgery, the enhanced recovery programs have been developed and described in great

details in the literature (Fearon et al., 2005; Lassen et al., 2009). Lately, the ERAS[®] Society has published evidence-based guidelines for perioperative care in elective colon surgery and rectal/pelvic surgery (Gustafsson et al., 2013; Nygren et al., 2013).

Short-term Benefits of ERP on Colorectal Cancer Surgery

In 2013, a meta-analysis of 13 randomized controlled trials comparing ERP and traditional care for various colorectal operations including colorectal cancer surgery revealed that patients under the care of ERP had approximately 2.4 day lesser hospital stay and a 30% reduction in postoperative complications. There was no difference in 30-day mortality and readmission between the two groups (Zhuang et al., 2013). Two recent systematic reviews also confirmed the advantages of ERP over conventional care for lower gastrointestinal surgery (Spanjersberg et al., 2011) and a variety of surgical disciplines including colorectal cancer surgery (Nicholson et al., 2014).

Interestingly, ERP further shortened the length of hospital stay in patients undergoing laparoscopic colectomy (Vlug et al., 2011; Haverkamp et al., 2012) and laparoscopic total mesorectal excision for rectal cancer (Huibers et al., 2012). A recent meta-analysis of ERP in laparoscopic colorectal resection for colorectal malignancy demonstrated that the ERP was safe and effective in reducing length of hospital stay and overall complication rates (Li et al., 2013). Moreover, patients under the ERP pathway had a faster recovery of bowel function (Jottard et al., 2008; Huibers et al., 2012). However, the optimal outcomes of ERP were largely dependent on the compliance and adherence of the protocol (Gustafsson et al., 2011; Cakir et al., 2013).

Potential Long-term Benefits of ERP on Colorectal Cancer Surgery

Although the advantages of ERP have been widely reported in various operations of colorectal diseases and known to provide increased benefits to patients during the postoperative recovery period, the impact of such a program exclusively on the long-term oncological outcomes of colorectal cancer surgery is lacking. Emerging evidence indicates that the application of ERP in colon cancer surgery effectively inhibited release of post-operative inflammatory cytokines and mediators, with a reduction in perioperative stress and a preservation of post-operative immune system (Wang et al., 2012). It was suggested that the better preservation of host immunity might be related to better anti-tumor activity and may increase survival in advanced colon cancer (Karanika et al., 2013).

Also, patients undergoing colorectal surgery using the ERP pathway had a shorter convalescence after surgery and had a reduction in rates of overall postoperative complication; mainly a lower incidence of medical complications (Zhuang et al., 2013). Postoperative complication is one of major predictors to delay or

omit adjuvant chemotherapy for colon cancer patients; particularly those with serious complications such as renal failure, pneumonia and anastomotic leakage (Merkow et al., 2013). Surprisingly, even minor complications like superficial surgical site infection could lead to a significant delayed time to chemotherapy. It was evident that, in patients with stage III colon cancer, a delay in initiation of adjuvant chemotherapy was correlated with poorer overall survival and cancer-specific survival (Hershman et al., 2006). Interestingly, a systematic review and meta-analysis by Biagi and colleagues demonstrated that a 4-week increase in time to adjuvant chemotherapy was associated with a 14% decrease in both overall survival and disease-free survival of colorectal cancer patients (Biagi et al., 2011). In a Swedish cohort study, adjuvant treatment initiated beyond 8 weeks after surgery appeared to have no benefit when compared with surgery alone for stage III colon cancer (Berglund et al., 2008).

As a result, many guidelines including those from the European Society of Medical Oncology (ESMO), have suggested to start adjuvant chemotherapy in colorectal cancer patients with nodal involvement as early as possible after surgery (preferably within 12 weeks) (Schmoll et al., 2012). Therefore, the ERP could be one of modern perioperative care pathways to enhance patient's recovery, to minimize postoperative morbidity, and to improve surgical and oncological outcomes of colorectal cancer surgery.

Current Situation of ERP in Colorectal Cancer Surgery

The ERP in colorectal cancer surgery has been well adopted into daily surgical practices. A survey of experienced colorectal surgeons representing 123 centers worldwide in 2011 showed that 63% of respondents used ERP strategies within their surgical management of rectal cancer; European surgeons tended to apply ERP more frequently than US surgeons (Augestad et al., 2011). Another recent survey indicated that 37% of colorectal surgeons in Australia and New Zealand employed ERP strategies (Kahokehr et al., 2011). It was evident that ERP was cost-effective in the treatment of colorectal diseases (Lemanu et al., 2014).

Whilst the robust evidence of ERP is increasingly growing in various operations of alimentary tract surgery including colorectal cancer and hepatobiliary malignancy (Gustafsson et al., 2013; Lassen et al., 2013; Nygren et al., 2013), main barriers to implementing ERP included lack of support from institutions and colleagues (Kahokehr et al., 2011). Multidisciplinary team approach and regular review could help integrating ERP into daily surgical practices aiming to improve the outcomes of patients with colorectal cancer. So far, the application of ERP in colorectal surgery was associated with some improvement in patient's health-related quality of life (Khan et al., 2010).

Conclusions

The short-term benefits of ERP for colorectal cancer surgery is well documented in terms of shorter length of

Table 1. Summary of Potential Benefits on Short-term and Long-term Outcomes of Colorectal Cancer Surgery using an Enhanced Recovery Program (ERP)

| Short-term outcomes | Long-term outcomes |
|---|--|
| <p>STRONG evidence (from several meta-analyses and systematic reviews):</p> <ul style="list-style-type: none"> •Shorter hospital stay •Fewer complications •Faster recovery of bowel function •Better quality of life | <p>NO direct evidence, but potential benefits on cancer treatment may be related to:</p> <ul style="list-style-type: none"> •Preservation of host immunity •Shorter time from surgery to start adjuvant chemotherapy •More likely to initiate and complete course of adjuvant therapy |

hospital stay, faster recovery of gastrointestinal function, and fewer incidence of postoperative complication when compared with conventional postoperative care. Long-term measures of such a program in colorectal cancer are needed. Theoretically, ERP might be of oncological benefit in colorectal cancer patients because it could enhance patient's recovery, maintain integrity of postoperative immune system, increase feasibility of postoperative chemotherapy, and shorten time intervals from surgery to chemotherapy. The summary of potential benefits on the short-term and long-term outcomes of colorectal cancer surgery using ERP is shown in Table 1. Since there are no reports examining the long-term results of the application of ERP in colorectal surgery in the literature, the investigation of oncological outcomes of ERP in colorectal cancer surgery should be encouraged.

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