Published in final edited form as:

J Gastrointest Surg. 2018 January ; 22(1): 164–171. doi:10.1007/s11605-017-3605-9.

What is ‘Enhanced Recovery’, and How Can I Do It?

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Keywords

ERAS; Enhanced Recovery After Surgery; fast-track

INTRODUCTION

Enhanced recovery (ER) and fast-track protocols were initially implemented in the perioperative management of the surgical patient over 20 years ago.[1] Although ER originated in colorectal surgery, it has been broadly adapted to most surgical specialties. Common ER end points, which are routinely measured and improved with its utilization, include shortened length of stay, improved functional outcomes, and decreased costs.[2] Several clinical trials and meta-analyses support individual elements of ER pathways as well as their positive effects when compounded.[3,4]

Patient education and engagement are the foundation of all ER programs. Moreover, a multi-disciplinary approach is necessary to support this foundation with four fundamental perioperative care principles that include: early feeding, early ambulation, goal directed fluid therapy, and opiate-sparing analgesia (Figure 1). The following is a review of several important domains of modern ER protocols, with additional content reflecting our institutional experience with frailty evaluation and Enhanced Recovery implementation across 13 oncologic diseases and over 6,000 cancer patients.

CORE COMPONENTS OF THE ENHANCED RECOVERY PATHWAY

Preoperative Evaluation and Patient Education

A complete history and physical exam should review all comorbid conditions, uncontrolled medical conditions, and previous surgical procedures. In the oncology patient, a thorough oncologic history reviewing radiation therapy, neoadjuvant cytotoxic/biologic chemotherapy, and future plans to receive adjuvant therapy should be conducted.

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Financial Disclosures: None

Disclosure Information: **Authors:** Thomas A. Aloia, M.D. has nothing to disclose. Bradford James Kim, M.D., M.H.S. has nothing to disclose. **Editors-in-Chief:** Richard A. Hodin, M.D., Timothy M. Pawlik, M.D., MPH, PhD has nothing to disclose. **CME Overseers:** Arbiter: Timothy M. Pawlik, M.D., MPH, PhD has nothing to disclose; Vice-Arbiter: Melanie Morris, M.D., has nothing to disclose; Question Reviewers: Michael Anthony Edwards, M.D has nothing to disclose; F. Andrew Morfesis, M.D., has nothing to disclose.

Before surgery, chronic medical conditions contributing to borderline medical operability should be optimized.[5] For example, patients with uncontrolled diabetes are at significant risk for adverse postoperative outcomes including wound infections, organ space infection, and tumor recurrences. Additionally, functional status should be graded with either the Eastern Cooperative Oncology Group (ECOG), Karnofsky or another validated scoring system. Functional capability can be further quantified with the 6-minute walk test, timed up and go test and with various patient reported outcome tools.[6–10] Identifying correctable deficits will guide prehabilitation efforts, including preoperative physical conditioning (Figure 2), nutritional counseling, blood glucose control, and smoking cessation. The findings of a frailty evaluation do not exclude a patient from participation in an enhanced recovery protocol, but they do help the team predict the ability of a patient to comply with all of the elements and to properly resource the inpatient and early outpatient recovery process.

Patient education and counseling are paramount for successful ER. The patient should be educated and given information about the indicated operation. Additionally, education materials and counseling should be provided to discuss enhanced recovery principles and goals. This will give an opportunity for the caregiver and patient to focus on awareness of potential surgical complications and recovery expectations. In order for multimodal pain control, early ambulation, and timely discharge from the hospital to be successful, patients must be adequately educated and properly aligned with expectations to allow for appropriate planning.[11] The education material provided encompasses a broad spectrum of topics, which may be overwhelming to the patient. Therefore, all conversations must be done in the patient's language of choice and supplemented with written information that reiterates the counseling sessions. Following patient education, patients should be provided ample opportunity to ask their surgical team questions prior to agreement on the surgical/analgesia plan. Depending on institutional resources and historical norms the responsibility for education may be under the purview of surgeons, trainees, outpatient nurses, or other navigators. There are no data available suggesting that this education is better received by the patient from any one of these resources. Utilizing multiple methods of education improves compliance and decreases patient anxiety prior to surgical intervention.[12]

Nutrition

Preoperative evaluation of the patient's nutritional status is an important component of the preoperative assessment. Both weight loss and obesity are potential risk factors that can be stratified and addressed. In the cancer patient, neoadjuvant therapy puts patients at risk for malnutrition, weight loss, and sarcopenia. Laboratory tests should include albumin, pre-albumin, and/or ferritin. Albumin lower than 3.5 g/dL and pre-albumin less than 18 mg/dL are both accurate predictors for postoperative morbidity.[13,14] Additionally, both sarcopenia and sarcopenic obesity should be identified, as these measurements of frailty are, likewise, associated with both morbidity and mortality.[15] Identification of preoperative malnutrition and frailty is worthwhile, as preoperative optimization of nutrition has been associated with improved outcomes.[16]

Immediately prior to surgery, patients have historically been asked to endure a long period of fasting. More recently, these traditional norms have been challenged. More and more, patients without gastroduodenal impairment are being given clear liquids up until 2 hours prior to anesthesia induction. These recommendations are in accordance with American Anesthesiologist's Association (ASA) guidelines on fasting to promote maintenance of euvolemia and glycemic balance.[17] Although there continues to be controversy surrounding the role of bowel prep in elective colorectal surgery, there appears to be no benefit of bowel prep prior to liver surgery.[18]

An additional consideration in the preoperative nutrition regimen is the implementation of carbohydrate loading. Some evidence exists in favor of preoperative carbohydrate loading because it supports energy stores for postoperative healing and maintains even glycemic balance in diabetic patients. Decreased postoperative insulin resistance, patient discomfort, and improved healing are all benefits reported with carbohydrate loading.[19–21] If utilized, a solution of 100 g of carbohydrates should be administered the evening prior to surgery with an additional 50 g solution administered the morning of surgery. To meet this need various groups have tried to balance cost and availability (ie. Apple juice) with complex commercial products with particular efficacy (ie. Maltodextran content and immune-adjuvants).

Perioperative Antimicrobial Prophylaxis

In accordance with Surgical Care Improvement Project (SCIP) guidelines, antimicrobial prophylaxis is administered perioperatively to prevent postoperative infections. The majority of patients should be administered intravenous antibiotics per a protocol within the hour prior to surgical incision and redosed as indicated during the operation to maintain coverage. [22,23] Gram negative and anaerobic organism coverage should be considered when there is potential for intraabdominal contamination. All antibiotics should be stopped within 24 hours of surgery with the exception of patients with a documented source of infection that requires further treatment. Chlorhexadine-alcohol 2% solution or betadine-alcohol are preferred over povidone-iodine alone for skin preparation.[24]

Perioperative Analgesic Agents

There are multiple reports in the literature on the negative effects opioids can have on patient function and on cancer biology.[25–29] Emerging data points to direct opioid-cellular interactions that explain these observations. Opiates have been reported to activate vascular endothelial growth factors (VEGF), directly stimulating cancer growth and metastatic potential.[25–27,30] Moreover, worse survivals in patients with breast and lung cancer were reported when the tumors expressed certain polymorphism of the μ -opioid receptor (MOR). [28,29] Lennon et al reported that overexpression of MOR in human non-small cell lung cancer increased primary tumor growth and metastasis in xenograft models. Additional studies from Lennon et al focused on the effects of MOR on epithelial mesenchymal transition (EMT), [26] which is a necessary oncogenic process involving loss of cell-cell adhesion, subsequent loss of baso-apical polarization, cytoskeletal remodeling, and increased cell motility and transcription factors for cancer cell growth and metastasis.[31–34] They showed that MOR regulates opioid and epidermal growth factor (EGF) signaling,

which is important for human NSCLC cell proliferation and migration; moreover, human NSCLC cells treated with opioids exhibited an increase (snail, slug, vimentin) and decrease in other (ZO-1 and claudin-1) protein levels consistent with an EMT phenotype.[26] In summary, these results suggest that opioid-MOR interactions may have a direct effect on the proliferation, migration and EMT transition for cancer progression. These findings have led to human clinical studies investigating the effects of analgesia agents on cancer outcomes including recurrence and overall survival.

Opiate-sparing analgesia strategies are a corner stone of ER and are most effective when the approach is multimodal. When executed effectively, these protocols result in less intraoperative and postoperative need for narcotics. When patients have a history of chronic narcotic use or exposure, preoperative consultation with pain management specialist should be considered.

Preventive strategies to manage post-surgical pain can be initiated in the preoperative holding area. Administration of non-narcotic neuromodulators such as oral pregabalin, gabapentin, NSAIDs, and opiate-like narcotics (e.g. tramadol) in combination are common regimen choices. In conjunction, pre-emptive pain control with neuraxial blocks and field blocks (e.g. transversus abdominus plane [TAP] block or epidural catheter) can limit the need for intraoperative and postoperative narcotic use. In addition to their impact on acute pain control, non-narcotic pain controlling medications, such as NSAIDs and acetaminophen, may decrease the risk of cancer progression.[35–38]

Goal Directed Fluid Therapy

During surgery, goal directed fluid therapy (GDFT) involves the use of parameters found in hemodynamic indices such as stroke volume variation (SVV) and/or pulse pressure variation (PPV) to give the appropriate amount, type, and timing of fluids. GDFT has been shown to decrease morbidity, mortality, and costs.[39] There are multiple non-invasive and partially invasive (e.g. Esophageal probe) technologies available to measure these parameters. Ultimately, response to fluid challenge is an optimal way to employ these technologies as a dynamic assessment of true intravascular volume status during surgery.

Both during and after surgery, static measurements of systemic blood pressure, traditional hemodynamic indices (ie. central venous pressure, pulmonary capillary wedge pressure), and urine output have substantial limitations in the reliable measurement of intravascular volume status. Other novel metrics that accurately assess intravascular volume status include the measurement of serum brain natriuretic peptide (BNP).[40,41] BNP is a 32-amino acid protein produced by the cardiac atria and ventricles in response to dilation from volume expansion and pressure overload.[40,42] Once in circulation, BNP promotes diuresis, natriuresis, reduction of preload, and afterload through the binding of guanylate cyclase receptors on endothelial cells. A BNP-guided fluid protocol typically includes daily postoperative measurement of BNP level. If BNP is <100 pg/mL or urine output is decreased to <50 mL/2 hour, a 250–500 mL bolus is administered with no change in maintenance fluid rate. If BNP is between 100–200 pg/mL, no bolus is required, and maintenance intravenous (IV) fluids are minimized. Lastly, if BNP is elevated above 200 pg/mL, maintenance IV fluid rates are minimized or stopped with the consideration of diuresis and/or work-up for

diastolic heart failure. The utilization of serum BNP-guided volume management is superior to traditional chemistry and bedside volume assessment; moreover, data from Patel et al, at MD Anderson Cancer Center, have demonstrated reduced cardiopulmonary/renal complication rates from 4.0% in the pre-protocol group to 0.9% after initiation of the BNP-guided hepatobiliary fluid protocol ($p=0.04$, HPB 2017, *in press*).

Urinary catheters are routinely used in many major abdominal operations due to the length of procedure as well as for urine output monitoring to facilitate GDFT both during the operation and the immediate recovery period. The moment patients are ambulatory postoperatively, typically postoperative day (POD) 1 or 2, indwelling urinary drainage catheters should be removed. If hourly urinary output monitoring is required, the surgical team should frequently reassess its need so that the catheter may be removed as soon as possible. In older males with urinary retention, tamsulosin can be pre-emptively administered to avoid urinary retention and need for catheter replacement.

Postoperative Mobilization

Ambulation should be initiated early in postoperative period, and it is a core component of ER. Although a simple part of patient care, its practice can have profound effects on reducing ileus, improving pulmonary function, and decreasing the risk of postoperative thromboembolic events. Limiting extraneous drains, IV tubing, and urinary catheters can help facilitate early mobilization by reducing physical barriers to activity. Physical and occupational therapists should be involved early in the hospitalization for patients with baseline deficits of ambulation and mobility.

Venothromboembolism Protocol

Despite the availability of venous thromboembolism (VTE) guidelines, [43–45] national rates of postoperative venothromboembolism continue to be reported at high levels.[46,47] Preoperatively, TED hose and sequential compression devices (SCD) should be placed and activated prior to anesthesia induction; they are discontinued once early ambulation is accomplished.[48] The first dose of anticoagulant VTE prophylaxis (usually unfractionated heparin) should be initiated prior to incision. Between POD 1 and 3, patients are usually converted to daily subcutaneous enoxaparin for the remainder of the hospitalization. Equally important, anticoagulation is recommended to be continued for a total of 28 days from the date of surgery after major open abdominal surgery. These recommendations are supported by ERAS Society guidelines.[23]

Postoperative Diet

After most routine gastrointestinal operations, diets should not be limited. Furthermore, the routine use of nasogastric tubes for enteric drainage should be avoided to promote early advancement of diet, faster ambulation, and easier maintenance of euolemia/electrolyte levels. Individuals without contraindication to early *per os* should be ordered clear liquids on the same day of surgery with plans for a regular diet the next morning. Full liquid diets are avoided because 30% of patients are lactose intolerant, and they generally delay diet advancement, unnecessarily prolonging length of stay. IV fluids should be used judiciously and only be given when the patient is unable to sustain euolemia with oral liquids.

Although not supported by level one evidence, it is generally accepted that maintenance IV fluids should be discontinued when the patient has taken approximately 600 mL of oral intake. If enteric drainage is required after surgery with a nasogastric tube, this should be removed as soon as possible in the postoperative course. To limit postoperative nausea/vomiting and promote an early postoperative diet, nausea prophylaxis should be administered in the operating room, prior to extubation. Additionally, corticosteroids such as dexamethasone are administered prior to incision as another preventive strategy for nausea and to blunt the perioperative stress response.

Patient Reported Outcomes and Return to Intended Oncology Therapy (RIOT)

For cancer patients, the two main goals of enhanced recovery are a rapid return to normal life function and to adjuvant cancer therapies. Studies of ER pathways have proven superiority with classic surgical outcomes such as decreasing LOS, morbidity, mortality, and costs.[3,4] In addition, reports have shown ER improves functional status measured by validated patient reported outcome tools.[49] In the cancer patient, return to intended oncologic therapy (RIOT) is an important quality metric that validates the degree of successful recovery.[50]

Team Building, Buy In, and Compliance Monitoring

Implementing a successful ER program requires participation from all facets of patient care: the patient and family, anesthesia, surgery, nursing, pharmacy, nutrition, trainees, and hospital administration. In order for all of these team members to buy in to the patient oriented goals of ER, all must understand the principles and believe in these changes. For the care team, education in the form of lectures, problem based learning, and information packets should all be utilized; furthermore, this initial process should be supplemented with up to date research findings from the ER literature. Once a system is in place, subsequent monitoring should occur to evaluate both compliance and effectiveness. In turn, this collaborative effort to build a system that effectively implements ER to patient pathways produces a more cohesive team and higher provider satisfaction.[51]

CONCLUSIONS

ER is a multimodal (Table 1) approach that minimizes the physiologic impact of surgery and anesthesia.[49] All the techniques and agents described focus on reducing the stress response, providing an environment that promotes recovery. ER is most successful when patient education and expectations are thoroughly addressed, combined with a multi-disciplinary/modal approach implemented via systematic preoperative and postoperative order sets.

Acknowledgments

Funding Sources: Dr. Bradford Kim is supported by National Institutes of Health grant T32CA009599

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Learning Objectives

1. Define Enhanced Recovery in Surgery
2. Understand all goals of enhanced recovery
3. Discuss several key components of Enhanced Recovery
4. Understand the team based approach and buy in required to successfully execute Enhanced Recovery

Figure 1.

Enhanced Recovery sits on a foundation of patient education and engagement. Four perioperative fundamental strategies that support the program are early feeding, goal directed fluid therapy, non-narcotic analgesia, and ambulation.

Figure 2.

The identification of deficits in neurocognitive, nutritional and physical functional status creates an opportunity for prehabilitation to be implemented. Prehabilitation increases the preoperative clinical reserve, and when combined with Enhanced Recovery programs, can increase the safety of surgery.

Table 1

Enhanced Recovery in Liver Surgery vs. Traditional Pathway, previously reported by Day et al.

Factors		Enhanced Recovery	Traditional
Pre-operative	Education	Open and MIS liver surgery patient education material provided, as well as, ER Specific Patient Education material provided includes information about ER principles, patient and care-giver expectations and pain management.	Open and MIS liver surgery patient education material provided.
	Fluid Management	Saline lock IV in pre-op holding	KVO IV
	Preoperative Fasting	Solids up to 6 hours prior to surgery. Clear liquids permissible up to 2hrs before surgery	Clear liquids after lunch day prior to surgery, NPO post midnight.
	Bowel State	No mechanical bowel preparation required	Mechanical bowel preparation used selectively
	Preventive Analgesia	Celecoxib 400 mg PO, Pregabalin 75 mg PO (Avoid, Age>65), Tramadol ER 300 mg PO morning of surgery. Anxiolytics and anti-nausea medication as needed	Anxiolytics and anti-nausea medication as needed
Intra-operative	Perioperative Steroids	Dexamethasone 10mg intravenous on induction of anesthesia	No
	Opioid Sparing Anesthesia	Yes	No
	Total Intravenous Analgesia	Dexamethasone 10 mg IV at induction; IV Acetaminophen 1 gram q 6 hours; Propofol as main anesthetic agent; IV Dexmedetomidine; IV Ketamine; IV Lidocaine; Infusions titrated by anesthesiologists per patient as needed	Combined protocol with narcotics and inhalational agents
	Fluid Management	Goal directed: monitor stroke volume	Goal directed: unmonitored
	Regional Analgesia	MIS: Local anesthetic wound infiltration with long-acting liposomal bupivacaine. Open: Epidural preferred over PCA	MIS: Local anesthetic wound infiltration with short-acting lidocaine/bupivacaine. Open: Epidural or PCA
	Drains	Limit to only when absolutely indicated	Selectively used
Post-operative	Opioid Sparing Analgesia	Yes. Pregabalin 75 mg po BID, start pm POD0 × 48h; Acetaminophen 500 mg po x 1 POD0; Celecoxib 200 mg PO BID, start POD1; Tramadol 50mg PO q6h, start POD1 × 48h; Hydromorphone 0.5 mg IV q 30 minutes prn breakthrough pain not relieved within 30 mins of oxycodone; No PCA unless failure of Epidural.	Epidural, PCA hydromorphone, hydrocodone, acetaminophen
	PRN Analgesia	Epidural patient: titrated per pain service; Non-epidural patient: Mild pain (1–3): Acetaminophen 500 mg PO q6h; Moderate pain (4–6): Tramadol 50 mg PO q6h; Severe pain (7–10): Hydromorphone 0.5 mg q15 min x 2	hydromorphone, tramadol, hydrocodone and surgeon discretion
	Tubes	No NGT	Selective NGT
	Early Ambulation	Yes. Day of surgery: Sit on edge of bed; POD1 Out of bed to chair and ambulation at least 4 times daily	Yes. Day of surgery: Sit on edge of bed; POD1 Out of bed to chair and selective ambulation at least 4 times daily
	Fluid Management	Hepatobiliary fluid protocol, Minimize IVF rate, SL after 600cc PO	Hepatobiliary fluid protocol, Minimize IVF rate.
	Early Oral Intake	Patients allowed clear liquids on day of surgery. Regular diet POD1	NPO with Ice POD0, POD1 clears, POD2 regular
	Ready for discharge criteria	Formalized: Independently ambulatory, good pain control, tolerating diet, bowel function, no infections, comorbidities under control	At surgeon discretion