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EDITORIAL I

Enhanced recovery: more than just reducing length of stay?

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The concept of enhanced recovery (ER) after surgery is not new. It was pioneered in Denmark in the 1990s and in that time has been practiced under various names, including fast-track surgery and accelerated recovery. Currently, NHS improvement is leading a major initiative in the UK to implement ER across a number of specialities, including colorectal, musculoskeletal, urology, gynaecology, and breast surgery (http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/@ps/documents/digitalasset/dh_115156.pdf). The major evidence base to date is from colorectal surgery. It is noteworthy that in spite of anaesthesia having a pivotal role in driving ER forward, many of the publications are found in surgical journals.

There are many traditionally perceived benefits from ER, for patients, healthcare professionals, and hospital managers. Patients recover from surgery more swiftly and are able to resume their normal lifestyle more quickly. For healthcare professionals and managers, patients spend less time in hospital resulting in either more capacity or a reduced requirement for hospital beds and therefore cost. Of the many criteria used to judge ER, length of stay (LOS) is the most commonly used. It is widely collected and allows easy comparisons between units. Dramatic reductions in LOS have been described including 23 h stay laparoscopic colectomy.[1] However, there are several pitfalls associated with LOS. Time fit for medical discharge is probably a better marker but may not be the same in all hospitals and is not always the same as LOS, as it is recognized that patients may remain in hospital for reasons other than medical ones. In addition, some use the mean LOS, while others use the median LOS. This can be misleading; for example, in a group of patients in which a small number have a very prolonged LOS, the median LOS effectively ignores these patients. Despite these points, LOS (mean or median) is still so widely used that a reduction in LOS is almost seen as the *raison d'être* of ER.

There are, however, potentially more benefits other than having patients in hospital for less time. ER allows patients to recover quicker, using a number of techniques including preoperative carbohydrate loading, small incision surgery, reduced tubes, drains, etc., minimal use of opioid analgesia, avoidance of sodium and/or fluid overload, early resumption of enteral feeding, and early mobilization.[2] This has been encompassed into a protocol-driven care pathway ensuring great consistency in patient treatment, from the preoperative phase through to discharge. Importantly, it has been demonstrated that the greater adherence to ER protocols, the greater the improvement in clinical outcome.[3] Of all the steps that are important in colorectal surgery (some 20 in all), we have simplified them to analgesia, goal-directed fluid therapy (GDFT), and 'all the others' in the ER pathway and have termed this the trimodal approach.[4] Perioperative analgesia and i.v. fluid therapy are generally under the control of the anaesthetist. The rewards are great if these processes are performed well but can be disastrous for patients if they are poorly conducted. Inadequate analgesia can result in poor mobilization, sleep deprivation, and ultimately an exaggerated stress response, or side-effects from excessive or inappropriate medication. The optimum analgesic regimen for many types of surgery is often contested.

Multimodal, opioid-sparing analgesia is seen as the gold standard since its description some 20 yr ago. The classes of drugs used have increased from paracetamol and anti-inflammatory drugs and weaker opioids and now includes many more drugs such as clonidine, gabapentin, lidocaine (*vide infra*), and magnesium.[5] Another key area is the use of nerve block for open colorectal surgery. Thoracic epidural analgesia has many advantages including a reduction in the pituitary, adrenocortical, and sympathetic responses to surgery. Several meta-analyses have provided encouraging results for the use of epidurals in major surgery, including a reduction in mortality, and a reduced incidence of deep vein thrombosis, pulmonary embolism, blood transfusion requirements, pneumonia, and respiratory depression. Other beneficial effects of epidurals are opioid sparing, a reduction in postoperative nausea and vomiting, and speedy return of normal gastrointestinal (GI) and muscular function.[6] However, with the adoption of newer surgical and anaesthetic techniques, the optimum analgesic regimen is less clear, in particular for laparoscopic colorectal surgery.[7] We have found spinal anaesthesia more beneficial than epidural in reducing LOS[8] and for facilitating 23 h stay.[1] However, although there was demonstrable opioid sparing, this did not affect the LOS of spinal anaesthesia patients[8 9] when compared with those receiving patient-controlled analgesia with morphine. Others have achieved opioid sparing with other less invasive nerve block, including transversus abdominis plane (TAP) blocks, rectus sheath catheters, and wound infiltration with local anaesthetic.

GDFT requires monitoring of stroke volume to guide i.v. fluid therapy. Too little fluid can result in inadequate oxygen delivery and too much may result in salt and water overload and oedema (in both peripheral and gut tissues). Both extremes will ultimately impair tissue oxygenation. Intensivists have stressed, for many years, the benefits of using fluids (and sometimes inotropes) to maximize oxygen delivery (DO_2), commonly using a figure >600 ml min^{-1} m^{-2}. Above this level, perioperative complications are reduced, presumably as adequate organ perfusion prevents GI complications. For laparoscopic surgery, as cardiac index and hence DO_2 is reduced due to pnemoperitoneum, we have recently described >400 ml min^{-1} m^{-2} to be a useful threshold in reducing complications.[10] However, not all clinicians have found GDFT to be advantageous,[11]and indeed the whole validity of the concept has been questioned.[12]

However, the overwhelming consensus is that meticulous adherence to perioperative fluid administration is very effective. Although old traditions may be hard to eradicate, the use of a preoperative carbohydrate drink and restriction of fluids were the two major independent predictors of improved outcome, with a 25% lower risk of postoperative complications and nearly 50% lower risk of postoperative symptoms delaying discharge.[3] This article serves to remind us of the detrimental effects of poor implementation of ER pathways which, when addressed, produces a marked improvement in outcome. The prevention of postoperative fluid overload cannot be overemphasized: for every litre of fluid administered, postoperative complications (mainly cardiorespiratory) increased by 32%,[3] and every litre of fluid resulted in an increased hospital stay of ~24 h.[8] Moreover, the wide acceptance of GDFT has resulted in its incorporation into the Department of Health's recent document innovation, health, and wealth (http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_131784.pdf).

So what are the other advantages of strict attention to ER protocols (and in particular analgesia and fluid balance) within ER programmes?

Reduction in complications

Patients in ER programmes are better prepared for surgery, have improved perioperative care, and complications can be reduced by up to 50%.[13] The early return of gut function reduces catabolic response and muscular dysfunction. Moreover, early mobilization helps to prevent pulmonary dysfunction and thromboembolism. In addition, wound infections are reduced by more than half for laparoscopic *vs* open colorectal surgery.

Reducing complications is pivotal, as it not only affects short-term morbidity and mortality, but also impacts on long-term outcomes. Previously, it was envisaged that any complications impacted on hospital stay alone and, once treated, these patients would then rejoin the cohort of patients who had not had complications. This is not the case: complications within 30 days are more important than both preoperative risk and intraoperative factors in determining survival after major surgery. Complications in this timeframe reduced survival by 69%—from 18.4 to 5.6 yr.[14]

Reduction in stress response

The classical endocrine, metabolic, and inflammatory responses, once viewed as a prerequisite to surviving major surgery, is more often regarded as detrimental, especially in excess. Massive catecholamine release, protein loss, hyperglycaemia, systemic inflammatory response, and marked immunosuppression (from both neuroendocrine activation and cytokine reduction) will not aid recovery. There are many approaches that can alter aspects of the stress response. Appropriate analgesia (especially regional anaesthesia) and GDFT can, independently, affect this process. More recently, it was recognized that other methods may reduce aspects of the stress response and include glucocorticoids, gabapentinoids, peripheral opioid antagonists, intraoperative warming, and early oral nutrition.[6] Immune function analysis from the LAFA trial has recently demonstrated that immune competence was preserved best in patients undergoing laparoscopic bowel resection with fast-track surgery, compared with laparoscopic surgery alone or fast-track open surgery alone, and all were superior to non-fast-track open surgery.[15] This preservation of immune competence may result in better long-term outcome, particularly if handling circulating tumour cells in the immediate postoperative

period. This potential benefit for patients with malignancy is described below.

Effect on cancer outcome

If anaesthetic techniques were to significantly improve cancer outcome, it would represent a major advance for the speciality. There is emerging evidence to support this theory, and the area was recently reviewed[16] and the relationship between cell-mediated immunity, in particular the role of natural killer (NK) cells, in tumour cell handling was described. For example, regional anaesthesia has been shown to increase survival in breast and prostate cancer surgery. A number of mechanisms were postulated including an opioid-sparing effect (morphine suppresses NK activity in animals) and a reduction in neuroendocrine stress response, enhancing immunity. The stress response analysis from the LAFA trial[15] adds further evidence. However, long-term follow-up of patients enrolled in the MASTER trial study found no evidence of improved cancer-free survival after the use of epidurals for abdominal cancers and therefore further evidence is still awaited in this area.[17]

In addition, there is currently interest in the anti-tumour effects of lidocaine, found *in vitro*, which has recently been shown to demethylate DNA in breast cancer cell lines at clinically relevant concentrations.[16 18] These possible benefits may be further magnified, as patients within ER programmes may also be fitter for adjuvant treatment more quickly (e.g. chemotherapy).

Thus, the role of the anaesthetist within an ER programme is becoming broader as it may now be seen to play a part in both reducing postoperative complications and the stress response, the latter enhancing immunity, which in turn may impacts patients' short- and long-term survival. Therefore, the aim for this improved, evidence-based standard of care can no longer be satisfactorily described as just a reduced LOS.

Enhanced survival?

ER should be seen much more than enabling patients to leave hospital more swiftly. The long-term benefits from reduced stress response and complications may impact for years. Perhaps, ER should be measured far more broadly in terms of enhanced life expectancy and perhaps quality of life. Indeed, preliminary data from hip and knee replacement surgery within ER programmes have demonstrated a reduction in both 30 and 90 day death rate,[19] although this was not replicated for colorectal surgery.[13] However, enhanced survival, with improved quality of life, for patients with and without cancer, should be seen as the ultimate reward for all our patients within ER programmes.

Where next: training, research, and further applications

The evidence is growing that ER is effective. Further data from the LAFA study in colonic surgery demonstrate that the optimum results are obtained with ER *and* laparoscopic surgery, but even if open surgery is required, results are improved if this is undertaken within ER care.[20] However, it should be noted that in this trial, the outcomes were nevertheless suboptimal, possibly related to poor compliance with ER pathways. UK anaesthetists have been at the forefront in delivering ER, as the programme has evolved from a few isolated centres and specialities into a widely adopted national programme. There is a Professional Consensus, signed by many of the relevant professional bodies, that it has become a standard of care embedded into routine practice. However, in order to continue and grow, we must now ensure that training and education are promoted, both at undergraduate and at postgraduate level so that ER becomes a part of exam curricula, Continuing Professional Development, and perhaps even revalidation. Multidisciplinary training and practice—adopted successfully in other areas of medicine—is required here.

ER continues to need good quality data to persuade both commissioners and providers of its merit. Key areas continue to be preoperative assessment, analgesic regimens, and appropriate perioperative fluid management. Although the evidence for GDFT is compelling, there are few randomized controlled trials apart from epidurals and spinals to evaluate the best analgesic regimens in ER. Good trials on TAP blocks and rectus sheath blocks are required. A reduction in the stress response, whether by neural block or pharmacological methods, such as steroids[21] or statins,[22] requires further studies. Another area of research is to elucidate further the significance of enhanced immune function after laparoscopic surgery, as this may be translated into reduced postoperative infections and improved tumour cell handling. Lastly, there are a few studies supporting the use of ER in the elderly. In spite of a reduced physiological reserve and increased comorbidities, these patients nevertheless appear to derive benefits from the process.[23]

Finally, the concepts of ER may not be limited to elective surgery. Some of its principles, such as early nutrition and mobilization, removal of tubes, and patient counselling, may be of use in emergency orthopaedics, general surgery, and possibly medical patients and those requiring intensive care.

Declaration of interest

None declared.

References

1 Levy BF, Scott MJP, Fawcett WJ, Rockall TA. 23-hour stay laparoscopic colectomy. *Dis Colon Rectum* 2009; **52**: 1239–43

2 Fearon KCH, Ljungqvist O, Von Meyenfeldt M, *et al.* Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. *Clin Nutr* 2005; **24**: 466–77

3 Gustafsson UO, Hausel J, Thorell A, Ljungqvist O, Soop N, Nygren J. Adherence to enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. *Arch Surg* 2011; **46**: 571–7

4 Mythen MG, Scott MJP. Anaesthetic considerations for enhanced recovery. In: Francis N, Kennedy RH, Ljungqvist O, Mythen MG, eds. *Manual of Fast Track Recovery for Colorectal Surgery*. London: Springer, 2012; 49–72
5 Fawcett WJ. Pain control in ER. In: Francis N, Kennedy RH, Ljungqvist O, Mythen MG, eds. *Manual of Fast Track Recovery for Colorectal Surgery*. London: Springer, 2012; 95–109
6 Kehlet H, Mythen M. Why is the high-risk surgical patient still at risk. *Br J Anaesth* 2011; **106**: 289–91
7 Levy BF, Tilney HS, Dowson HM, Rockall TA. A systematic review of postoperative analgesia following laparoscopic colorectal surgery. *Colorectal Dis* 2010; **12**: 5–15
8 Levy BF, Scott MJP, Fawcett WJ, Fry C, Rockall TA. Randomized clinical trial of epidural, spinal or patient-controlled analgesia for patients undergoing laparoscopic colorectal surgery. *Br J Surg* 2011; **98**: 1068–78
9 Wongyingsinn M, Baldini G, Stein B, Charlebois P, Liberman S, Carli F. Spinal anaesthesia for laparoscopic colonic resection using an enhanced recovery programme: better analgesia, but no benefits on postoperative recovery: a randomized controlled trial. *Br J Anaesth* 2012; **108**: 850–6
10 Levy BF, Fawcett WJ, Scott MJP, Rockall TA. Intra-operative oxygen delivery in infusion volume optimized patients undergoing laparoscopic colorectal surgery within an enhanced recovery programme: effect of different analgesic modalities. *Colorectal Dis* 2012; **14**: 887–92
11 Challand C, Struthers R, Sneyd JR, *et al.* Randomized controlled trial of intraoperative goal-directed fluid therapy in aerobically fit and unfit patients having major colorectal surgery. *Br J Anaesth* 2012; **108**: 53–62
12 Ghosh S, Arthur B, Klein AA. NICE guidance on CardioQ oesophageal Doppler monitoring. *Anaesthesia* 2011; **66**: 1081–3
13 Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery. A meta-analysis of randomized controlled trials. *Clin Nutr* 2010; **29**: 434–40
14 Khuri SF, Henderson WG, DePalma RG, *et al.* Determinants of long-term survival after major surgery and the adverse effects of postoperative complications. *Ann Surg* 2005; **242**: 326–43
15 Veenhof AAFA, Vlug MS, van der Pas MHGM, *et al.* Surgical stress response and postoperative immune function after laparoscopy or open surgery with fast track or standard perioperative care. *Ann Surg* 2012; **255**: 216–21
16 Snyder GL, Greenberg S. Effect of anaesthetic technique and other perioperative factors on cancer recurrence. *Br J Anaesth* 2010; **105**: 106–15
17 Myles PS, Peyton P, Silbert B, Hunt J, Rigg JR, Sessler DI. Perioperative epidural analgesia for major abdominal surgery for cancer and recurrence-free survival: randomised trial. *Br Med J* 2011; **342**: d1491
18 Kirk P, Berger R, Hollman MW, Fiegl H. Lidocaine time and dose-dependently demethylates deoxyribinuleic acid in breast cancer cell lines *in vitro*. *Br J Anaesth* 2012; **109**: 200–7
19 Malviya A, Martin K, Harper I, *et al.* Enhanced recovery program for hip and knee replacement reduces death rate. A study of 4500 consecutive primary hip and knee replacements. *Acta Orthopaed* 2011; **82**: 577–81
20 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
21 Srinivasa S, Kahokehr A, Yu T-C, Hill AG. Preoperative glucocorticoid use in major abdominal surgery: systematic review and meta-analysis of randomized trials. *Ann Surg* 2011; **254**: 183–91
22 Chopra V, Wesorick DH, Sussman JB, *et al.* Effect of perioperative statins on death, myocardial infarction, atrial fibrillation, and length of stay. A systematic review and meta-analysis. *Arch Surg* 2012; **147**: 181–9
23 Krenk L, Rasmussen LS, Hansen TB, Bogø S, Søballe K, Kehlet H. Delirium after fast-track hip and knee arthroplasty. *Br J Anaesth* 2012; **108**: 607–11

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EDITORIAL II

Time to engage

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On November 7, 2012, the Science Museum in London will launch *Pain Less*—an exhibition, website, and series of public events on contemporary research in pain medicine and anaesthesia. It will be held in Antenna, the Science News gallery run by the Contemporary Science team. In its 11 month run, the exhibition is expected to attract more than a million visitors. It is the first major exhibition the Museum has held on our speciality in living memory and represents an unprecedented opportunity for the profession to engage with the public.

Details of the preliminary stages of the project were published last year as part of a national call for ideas and

ONLINE FIRST

Adherence to the Enhanced Recovery After Surgery Protocol and Outcomes After Colorectal Cancer Surgery

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Objectives: To study the impact of different adherence levels to the enhanced recovery after surgery (ERAS) protocol and the effect of various ERAS elements on outcomes following major surgery.

Design: Single-center prospective cohort study before and after reinforcement of an ERAS protocol. Comparisons were made both between and across periods using multivariate logistic regression. All clinical data (114 variables) were prospectively recorded.

Setting: Ersta Hospital, Stockholm, Sweden.

Patients: Nine hundred fifty-three consecutive patients with colorectal cancer: 464 patients treated in 2002 to 2004 and 489 in 2005 to 2007.

Main Outcome Measures: The association between improved adherence to the ERAS protocol and the incidence of postoperative symptoms, complications, and length of stay following major colorectal cancer surgery was analyzed.

Results: Following an overall increase in preoperative and perioperative adherence to the ERAS protocol from 43.3% in 2002 to 2004 to 70.6% in 2005 to 2007, both postoperative complications (odds ratio, 0.73; 95% confidence interval, 0.55-0.98) and symptoms (odds ratio, 0.53; 95% confidence interval, 0.40-0.70) declined significantly. Restriction of intravenous fluid and use of a preoperative carbohydrate drink were major independent predictors. Across periods, the proportion of adverse postoperative outcomes (30-day morbidity, symptoms, and readmissions) was significantly reduced with increasing adherence to the ERAS protocol (>70%, >80%, and >90%) compared with low ERAS adherence (<50%).

Conclusion: Improved adherence to the standardized multimodal ERAS protocol is significantly associated with improved clinical outcomes following major colorectal cancer surgery, indicating a dose-response relationship.

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Group Information: The Enhanced Recovery After Surgery (ERAS) Study Group members are listed at the end of this article.

ALTHOUGH INTERVENTIONS within enhanced recovery after surgery (ERAS) or fast-track programs have been shown to improve postoperative recovery in colorectal surgery,[1-4] universal implementation has not yet occurred.[5] One reason could be that ERAS programs are considered complex and resource demanding.[6] Another is that the ERAS concept as such possibly appears elusive because the relative contribution of each intervention in the program remains uncertain. Nevertheless, some of the elements in the ERAS program, such as omission of routine bowel preparation for colonic resections, no routine use of postoperative drains, early removal of nasogastric tubes, and early feeding and mobilization, have already been incorporated in traditional care.[5,7] Recently, a modified fast-track protocol (RAPID) with only 4 interventions,[8] instead of 20 in the ERAS program,[9,10] was also presented.

Introducing ERAS protocols usually requires a major shift in clinical routines, and many units may have difficulties in making all these changes at once. The effect of the different perioperative ERAS interventions as well as the importance of adherence to the protocol in terms of clinical outcomes, such as postoperative symptoms, morbidity, and length of stay (LOS), remain unclear.

See Invited Critique at end of article

In this prospective cohort study, we assessed the effect of an ERAS protocol relaunch project on protocol adherence and clinical outcomes. The aim was to investigate the importance of protocol adherence and the influence of different ERAS components for clinical outcomes following colorectal cancer surgery.

METHODS

STUDY SUBJECTS

Ersta Hospital in Stockholm, Sweden, is one of the original centers in the European ERAS Study Group. The ERAS protocol for colon and rectal surgery of this collaborative group[9,10] was first implemented in 2002. Clinical data, including protocol adherence and clinical outcomes, have been prospectively captured in the Web-based international ERAS Database from the start.[11] At Ersta Hospital, all patients undergoing elective major colorectal surgery are consecutively included in the ERAS protocol, which has been the standard of care since 2002. Because of unsatisfactory compliance, the ERAS protocol was relaunched on March 1, 2005, to improve several aspects of the protocol itself and the adherence to the program. Preceding the relaunch, during autumn 2004, a site visit to the pioneering unit at Hvidovre Hospital, Hvidovre, Denmark, helped identify key areas of potential improvement. These improvements concerned a large number of details in the perioperative care protocol, as well as strategies to increase adherence (eTable, http://www.archsurg.com). All patients who underwent a colon and/or rectal cancer resection in the period from 2002 to 2004 (January 1, 2002, to February 28, 2005) and 2005 to 2007 (March 1, 2005, to December 31, 2007) were registered in the database and are included in the study. During these 2 periods, the surgical staff, consisting of 7 senior consultants, anesthetists, and nursing staff, has remained largely unchanged. The research protocol was approved by the ethics committee at the Karolinska Institutet and carried out in accordance with the 1989 World Medical Association Declaration of Helsinki.

STUDY DESIGN

All patients were treated according to a standardized ERAS protocol.[9] Key components in this protocol were thoracic epidural analgesia (activated before onset of surgery and discontinued on postoperative day 2-4), preoperative oral carbohydrate treatment (a carbohydrate-rich, clear beverage, Nutricia Preop [12.5 g/100 mL^{-1} carbohydrates, 12% monosaccharides, 12% disaccharides, 76% polysaccharides, 285 $mOsm/kg^{-1}$]; Numico, Zoetermeer, the Netherlands)[12] up until 2 hours prior to surgery, and avoidance of preoperative oral bowel preparation and perioperative fluid overloading. Early oral diet (4 hours after surgery) and early mobilization (2 hours out of bed on the day of surgery and then 6 hours daily) were also part of the protocol. Altogether, 114 variables, including 21 key ERAS adherence variables, were recorded. Clinical data, including extent of postoperative mobilization, symptoms delaying discharge, length of hospital stay (LOS), and 30-day morbidity and mortality, were prospectively captured in the ERAS Database.[11] Daily dietary intake and fluid/energy balance were recorded.[13] Patients were considered fit for discharge using the following discharge criteria: postoperative pain adequately controlled with oral analgesics (visual analog pain score <40 of 100), intravenous nutrition or fluids no longer needed, mobilization (out of bed ≥ 6 hours daily), return of bowel function (stool or repeated flatus), and no complications in need of treatment in the hospital. Complications were diagnosed following the Veterans Administration Total Parenteral Nutrition Trial definitions and classifications.[14] All patients were examined by a surgeon at Ersta Hospital 2 weeks after discharge and interviewed by a trained nurse on postoperative day 30 to register any late-occurring complications. The definition of postoperative symptoms was symptoms that were not part of a complication and that clearly caused prolonged LOS (unspecified fever, pain, fatigue, constipation, dizziness, or diarrhea).

DATA ANALYSIS

Altogether, 464 consecutive patients in the first period (2002-2004) and 489 consecutive patients in the second period (2005-2007) were included in the study. Adherence to the ERAS protocol was assessed among these 953 patients and analyzed with regard to postoperative outcomes, both between as well as across the 2 periods.

Results are presented as mean (standard deviation), median, odds ratio (OR), and 95% confidence interval (CI) when appropriate. A 2-tailed *t* test was used for crude group comparisons of continuous variables and multiple linear regressions, for adjusted comparisons. Crude associations between categorical variables were analyzed with χ^2 tests or the Fisher exact test, as appropriate. Baseline characteristics were analyzed to determine the univariate predictors of the different outcome variables: postoperative symptoms, LOS, and 30-day postoperative morbidity including infection rates. Multiple logistic regression was then used to assess the adjusted association between specific interventions and each outcome.

The adjustment variables were age, sex, body mass index, American Society of Anesthesiologists score, surgical interventions, and laparoscopic/open surgery. When calculating adherence to the 12 preoperative and perioperative (day 0, day of surgery) ERAS interventions, the cut offs for adherence to the continuous variables were set as follows: intravenous fluid, colon, peroperative 2000 mL + postoperative 1000 mL = 3000 mL and rectum, peroperative 2500 mL + postoperative 1000 mL = 3500 mL; per oral fluid, more than 0 mL; intravenous kilocalories, less than 200 kcal; and per oral kilocalories, more than 0 kcal.

Adherence was calculated as the number of interventions fulfilled/12 (total number of preoperative and perioperative interventions). When calculating impact on an outcome, preoperative and perioperative interventions were added in the multiple regression model using stepwise modeling including all variables with a P value $<.15$. A P value $<.05$ was considered statistically significant. All data were analyzed using Stata version 10.0 (StataCorp, College Station, Texas).

RESULTS

CHANGES IN BASELINE CHARACTERISTICS, TYPE OF SURGERY, AND ADHERENCE

First, to assess the impact of increased adherence to the ERAS protocol, baseline characteristics and type of surgery were compared between periods. The 464 consecutive patients treated in 2002 to 2004 were at lower anesthetic risk compared with the 489 operated on in 2005 to 2007 (American Society of Anesthesiologists score of 1: 21.6% vs 14.5%; $P=.007$; American Society of Anesthesiologists score of 3: 14.6% vs 19.7%; $P=.048$). Another significant difference was a small increase in the proportion of patients operated on laparoscopically (**Table 1**).

A smaller proportion of both low anterior resection and Hartmann operations were performed in the second period compared with the first period, which in turn had a lower proportion of abdominoperineal resections ($P<.05$). Fewer patients underwent pelvic surgery in the second vs the first period (40.5% vs 47.6%; $P=.03$) (Table 1). In both periods, the surgical procedure with the highest rate of complications was abdominoperineal resection (46% vs 58.1% in the second and first periods, respectively).

Table 1. Patient Characteristics

	No. (%)		
	2002-2004 (n=464)	2005-2007 (n=489)	*P* Value
Age, mean (SD), y	69.3 (11.9)	69.0 (11.6)	.77[a]
BMI, mean (SD)	25.4 (4.3)	25.2 (4.4)	.60[a]
Male/female	231/233	237/252	.68[b]
ASA score, %			
1	21.6	14.5	.007[b]
2	63.1	64.4	.69[b]
3	14.6	19.7	.048[b]
4	0.7	1.4	.33[c]
Colorectal cancer	464 (100)	489 (100)	
Dukes stage C/D	192 (41.4)	191 (39.1)	.39[b]
Preoperative radiation	141 (30.4)	126 (25.8)	.11[b]
Complex group[d]	68 (14.7)	65 (13.3)	.52[b]
Laparoscopic surgery[b]	6 (1)	23 (5)	.002[c]
Peroperative bleeding, mean (SD), mL	363 (409)	366 (448)	.91[a]
Surgical procedure			
Right hemicolectomy	97 (21)	137 (28)	
Sigmoid resection	31 (7)	20 (4)	
Left hemicolectomy	23 (5)	39 (8)	
Anterior resection (10 cm above anus)	61 (13)	77 (16)	
Anterior resection (10 cm below anus)	128 (28)	89 (18)	
Abdominoperineal resection	49 (11)	94 (19)	
Hartmann operation	46 (10)	26 (5)	
Other	29 (6)	7 (1)	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
[a] Two-tailed *t* test.
[b] Pearson χ^2 test.
[c] Fisher exact test.
[d] The complex group refers to patients with additional intraoperative procedures (for example, small-bowel resection).

Table 2. Protocol Compliance

	No./Total No.[a] (%)		*P* Value
	2002-2004	2005-2007	
Preoperative compliance			
Preadmission counselling[b]	361/454 (79.5)	465/487 (95.5)	<.001[c]
Carbohydrate drink[b]	200/398 (50.3)	311/465 (66.9)	<.001[c]
Without bowel preparation[b]	66/446 (14.8)	322/481 (66.9)	<.001[c]
Without premedication[b]	100/463 (21.6)	289/486 (59.5)	<.001[c]
Active warming[b,d]	229/372 (61.6)	428/439 (97.5)	<.001[c]
EDA	446/464 (96.1)	475/487 (97.5)	.22[c]
Perioperative compliance			
Intravenous fluid day 0, mean (SD), mL[b]	5220 (1560)	3820 (1210)	<.001[e]
Per oral fluid day 0, mean (SD), mL[b]	550 (560)	790 (570)	<.001[e]
Intravenous kcal day 0, mean (SD), mL[b]	398 (193)	204 (159)	<.001[e]
Per oral kcal day 0, mean (SD), mL[b]	122 (308)	299 (379)	<.001[e]
Out of bed day 0, 2 h[b]	166/406 (40.9)	222/459 (48.4)	.03[c]
Oral nutrition supplements day 0[b]	51/413 (12.3)	271/476 (56.9)	<.001[c]
Postoperative compliance			
Intravenous fluid day 1-3, mean (SD), mL	2640 (2970)	2090 (2640)	.02[f]
EDA catheter removal, mean (SD), d	3.8 (2.4)	3.9 (2.5)	.31[f]
Urinary catheter removal, mean (SD), d	4.7 (3.8)	4.7 (3.6)	.49[f]
Per oral fluid day 1-3, mean (SD), mL	4320 (2330)	5220 (1990)	<.001[f]
Out of bed day 1, 6 h	61/260 (23.5)	111/404 (27.5)	.29[f]
Oral nutrition supplements day 1	85/433 (19.6)	276/485 (56.9)	<.001[f]
Solid food day 1	387/459 (84.3)	438/484 (90.5)	.008[f]
Without drip infusion day 1	150/457 (32.8)	286/485 (59.0)	<.001[f]
Contact with nurse day 7	304/416 (73.1)	466/486 (95.9)	<.001[f]

Abbreviations: EDA, epidural anesthesia; ERAS, enhanced recovery after surgery.
[a] The denominator represents values recorded in the database.
[b] The 12 ERAS interventions used in calculations of overall mean adherence.
[c] Pearson χ^2 test.
[d] By Bair Hugger; Arizant Healthcare, Eden Prairie, Minnesota.
[e] Two-tailed *t* test.
[f] Multiple linear and logistic regression adjusted for age, sex, American Society of Anesthesiologists score, body mass index, type of operation, and laparoscopic surgery.

Overall, the mean preoperative and perioperative (day 0) adherence to the 12 specific elements of the ERAS protocol increased from 43.3% among patients undergoing colorectal surgery in 2002 to 2004 to 70.6% in 2005 to 2007 ($P<.001$). Adherence to most of the postoperative intervention parameters also improved significantly (**Table 2**).

POSTOPERATIVE OUTCOMES BETWEEN PERIODS

Following an overall increase in mean preoperative and perioperative adherence to the ERAS protocol from 43.3% to 70.6% between study periods, the number of patients with at least 1 complication declined from 203 (43.8%) in 2002 to 2004 to 165 (33.7%) in 2005 to 2007 and the number of patients with symptoms delaying discharge also declined from 307 (66.2%) to 247 (50.5%) (**Figure 1** and **Figure 2**). Thus, a 27% increase in overall adherence to the ERAS protocol was associated with a 27% reduction in relative risk of any 30-day postoperative morbidity (OR, 0.73; 95% CI, 0.55-0.98) and a 47% reduction in relative risk of symptoms delaying discharge (OR, 0.53; 95% CI, 0.40-0.70), adjusting for confounding. Although the median LOS went from 7 days to 6 days with higher adherence to the ERAS protocol, this was not statistically significant ($P=.14$). However, the proportion of patients with LOS within the clinic target for abdominoperineal resections (<7 days) increased significantly from 35.4% to 46.8% (OR, 2.34; 95% CI, 1.01-5.38) between the first and second periods (adjusted for confounding) (Figure 1). The difference in proportion of patients with LOS within the clinic targets for colonic surgery (<3 days) (9.0% vs 12.7%) and low anterior resection (<5 days) (17.4% vs 22.7%) was not significant. No significant difference was found in the proportion of reoperations (10.6% vs 8.8%), readmissions (10.6% vs 10.2%), or 30-day mortality (1.3% vs 1.2%) between the first and second periods, respectively.

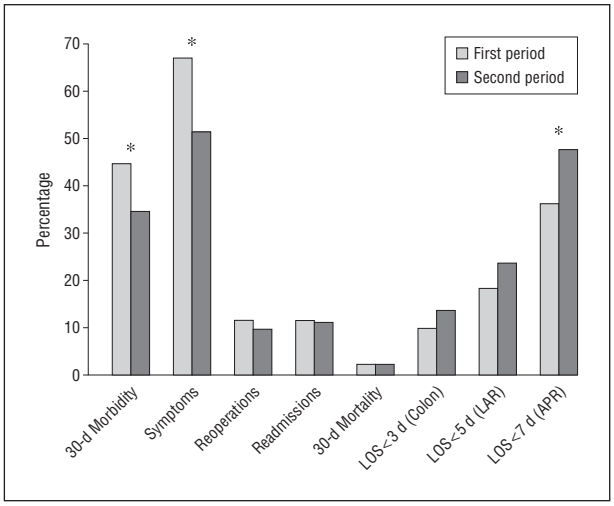

Figure 1. Postoperative outcomes. APR indicates abdominoperineal resection; LAR, low anterior resection; LOS, length of stay. *Statistically significant at $P<.05$.

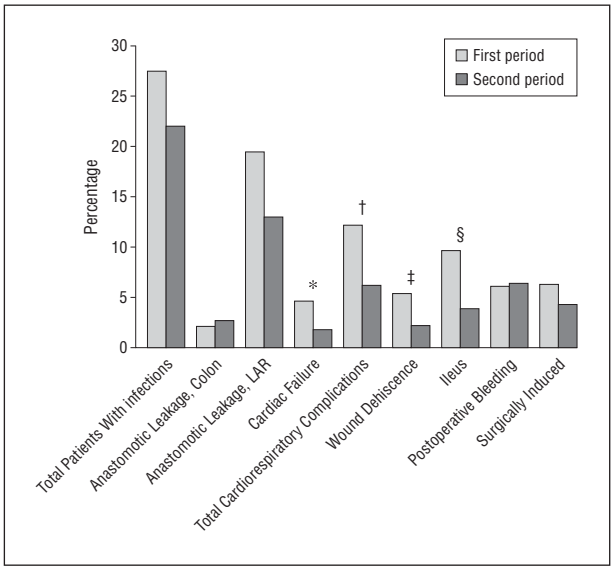

Figure 2. Postoperative complications in 2002 to 2004 (first period) vs 2005 to 2007 (second period). LAR indicates low anterior resection. *Odds ratio (OR), 0.34; 95% confidence interval (CI), 0.13-0.88; $P=.03$. †OR, 0.52; 95% CI, 0.31-0.87; $P=.01$. ‡OR, 0.31; 95% CI, 0.12-0.80; $P=.02$. §OR, 0.40; 95% CI, 0.21-0.76; $P=.005$.

POSTOPERATIVE OUTCOMES ACROSS PERIODS

The effect of overall adherence to the ERAS protocol, regardless of period, was also analyzed comparing patients with an overall adherence of more than 90% (n=76), more than 80% (n=183), and more than 70% (n=284) with patients with a low overall adherence less than 50% (n=333). Across periods, the proportions of patients with symptoms delaying discharge and 30-day morbidity were significantly reduced with higher levels of ERAS adherence using multivariate logistic regression adjusting for age, sex, American Society of Anesthesiologists score, body mass index, type of operation, and laparoscopic surgery (**Figure 3**). The ORs for postoperative symptoms were 0.35 (95% CI, 0.25-0.51), 0.34 (95% CI, 0.22-0.52), and 0.31 (95% CI, 0.17-0.55) with more than 70%, more than 80%, and more than 90% adherence, respectively. The ORs for 30-day morbidity were 0.62 (95% CI, 0.43-0.89), 0.57 (95% CI, 0.37-0.89), and 0.33 (95% CI, 0.16-0.66) with more than 70%, more than 80%, and more than 90% adherence, respectively, and the ORs for readmissions were 0.36 (95% CI, 0.17-0.76), 0.38 (95% CI, 0.15-0.95), and 0.16 (95% CI, 0.02-1.19) with more than 70%, more than 80%, and more than 90% adherence, respectively, vs less than 50% adherence.

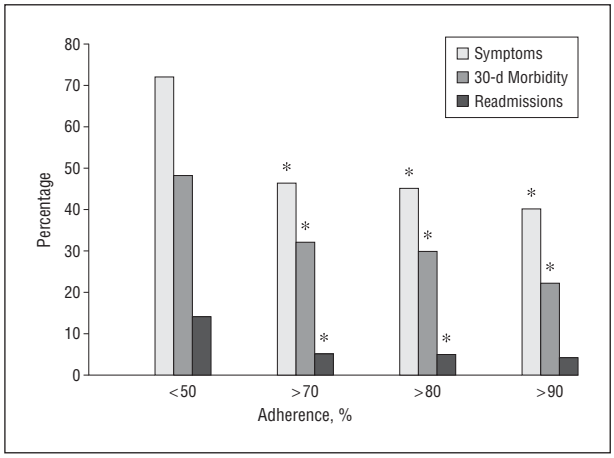

Figure 3. Association between adherence to the enhanced recovery after surgery protocol and postoperative outcomes. *Statistically significant at $P<.05$.

In univariate analysis, mean LOS was significantly shorter in patients with high ERAS protocol adherence (>70%, 7.4 days; $P<.001$; >80%, 7.0 days; $P<.001$; and >90%, 6.0 days; $P<.001$) compared with patients with low adherence (<50%, 9.4 days). Multiple regression revealed a significant difference in LOS among patients with adherence more than 90% ($P<.03$) vs less than 50% adherence, while the difference among patients with adherence more than 70% ($P=.07$) and more than 80% ($P=.08$) was borderline significant.

THE IMPACT OF SINGLE ERAS ELEMENTS

The effect of each intervention on postoperative symptoms, complications, and LOS was analyzed across periods. Multiple regression analysis adjusted for basic characteristics and other protocol interventions revealed that perioperative intravenous fluid management (intravenous day 0=day of surgery) (Table 2) and receiving a preoperative carbohydrate drink were major independent predictors of postoperative outcomes. The amount of fluids given the day of surgery was concurrently associated with preoperative oral bowel preparation. Patients receiving bowel preparation had a mean amount of 1000 mL of additional fluids given during the day of surgery (OR, 1.33; 95% CI, 1.14-1.54) while patients given preoperative carbohydrates received a mean 450 mL less fluids on average (OR, 0.75; 95% CI, 0.66-0.87). For each additional liter of fluids given during the day of operation, the risk of postoperative symptoms delaying recovery increased by 16% (OR, 1.16; 95% CI, 1.02-1.31) and the probability of postoperative complications increased by 32% (OR, 1.32; 95% CI, 1.17-1.50). In particular, fluid overload in-

creased the risk of cardiorespiratory complications (OR, 1.20; 95% CI, 1.10-1.31). If patients were treated with preoperative carbohydrates, the risk of postoperative symptoms was reduced by 44% (OR, 0.56; 95% CI, 0.40-0.77). In particular, preoperative carbohydrates significantly reduced the risk of postoperative nausea and vomiting, pain, diarrhea, and dizziness. Also, the risk of postoperative wound dehiscence was reduced by the preoperative carbohydrate drink (OR, 0.16; 95% CI, 0.05-0.50). Most of the other preoperative and perioperative ERAS interventions had a positive effect on the different outcome parameters, but the majority did not retain statistical significance in multivariate analyses adjusting for confounding.

COMMENT

In this large prospective observational study of more than 900 consecutive patients undergoing major surgery for colorectal cancer within an ERAS program, we found an association between improved protocol adherence and improved postoperative outcomes. Patients with high adherence to the ERAS protocol had a 25% lower risk of postoperative complications and nearly 50% lower risk of postoperative symptoms delaying discharge. They also had a higher tendency toward reaching LOS within the target limits compared with patients operated on under less optimal ERAS protocol adherence. Overall, there was a strong indication of a dose-response relationship between enhanced adherence to the protocol (>70%, >80%, and >90% compared with <50%) and improved surgical outcomes, reducing the relative risk for postoperative symptoms delaying discharge, 30-day morbidity, and readmissions between 38% and 69%. Nearly all preoperative and peroperative ERAS interventions influenced postoperative outcomes beneficially, but intravenous fluid management and intake of a preoperative carbohydrate drink were the major independent predictors.

It is possible, although unlikely, that factors other than improved adherence to the ERAS protocol could explain the observed differences in outcomes between periods. However, the turnover of surgical staff was minimal between periods. Second, although the mix of surgical procedures and the frequency of laparoscopy differed slightly between periods, the proportions of patients who underwent pelvic and laparoscopic surgery were adjusted for in the multivariate analysis. Also, because abdominoperineal resection, the procedure with the highest morbidity and longest recovery, was more frequent in the late study period, this would reduce the observed improvement in outcomes over time. However, the strongest argument for an independent association between overall adherence to the ERAS protocol and improved clinical outcomes is the indication of a dose-response relationship between level of adherence and postoperative morbidity, independent of study period.

The main explanation for the apparently high overall morbidity is that both major and minor complications were prospectively recorded, the patients were relatively old, and a large proportion underwent major pelvic surgery.

Several studies have demonstrated that the ERAS protocol is associated with earlier recovery and discharge after colonic resection,[15-22] while the recovery benefits following pelvic surgery remain uncertain.[20,23,24] It has not previously been convincingly shown that an ERAS protocol reduces postoperative complications after colorectal surgery, although 2 systematic reviews and 2 smaller uncontrolled studies[1,2,18,24] indicate a decline in surgical morbidity. It was recently found that a modest improvement in ERAS protocol adherence does not improve postoperative outcome,[25] but the present study shows a decline not only in complication rates and postoperative symptoms delaying recovery but also a shorter LOS following enhanced protocol adherence.

The ERAS protocol includes approximately 20 evidence-based care elements aimed at reducing surgical stress and postoperative catabolism.[9,10] We prospectively audited 21 index elements to assess protocol adherence, 18 of which were significantly improved after the program relaunch. Randomized studies on the importance of the different ERAS components are lacking and evaluating the impact of each single intervention is cumbersome since they influence each other, confounding interpretation. However, in the present study, most of the ERAS elements were found to significantly improve outcome parameters in univariate analysis but failed to do so after adjustment for confounding in the subsequent multivariate analysis where only 2 factors remained independent predictors: perioperative intravenous fluid management and preoperative carbohydrate treatment. Preoperative carbohydrate loading to avoid preoperative fasting reduces postoperative insulin resistance by approximately 50%[26] and attenuates postoperative nitrogen losses, lean body mass, and impairment of muscle function.[27-29] The carbohydrate drink, in addition to its metabolic effect, improves patient well-being (thirst, hunger, and anxiety) preoperatively.[30] We found that a carbohydrate drink not only reduced the need for perioperative intravenous treatment but also lowered the risk of postoperative symptoms delaying discharge by 44%. Moreover, fluid overloading in patients also played a major role, increasing the risk of postoperative complications by 32% for each additional liter of perioperative intravenous fluid administered. This is in line with previous reports of deleterious effects of fluid overload,[31,32] but our data show that controlling intravenous fluids is important even within an ERAS setting.

Despite the fact that the more complex multimodal ERAS programs repeatedly have been found to improve recovery after major surgery, old traditions prevail. Hoping to reach the same results with less effort, some clinics select a few components of the ERAS program and incorporate these into traditional care.[8,10] The RAPID protocol[8] is an example of a modified fast-track protocol where most of the enhanced recovery interventions are omitted. Using only 4 intervention arms (removal of tubes, ambulation, analgesia, and diet introduction), the protocol resulted in enhanced recovery after surgery. However, the target of removal of intravenous fluids on postoperative day 2, ambulation of more than 100 m on postoperative day 2, a patient-controlled analgesia pump instead of epidural anesthesia, and introduction of diet on postopera-

tive day 2 is a clinical pathway that differs from the multimodal pathway previously described by the ERAS Study Group.[10] As the enhanced recovery field develops, certain interventions may turn out to be nonessential. However, before omitting specific components in the protocol, such a decision should be based on a closer understanding of the importance of each element in the program. This study has shown that adherence to the ERAS protocol as a whole results in improved outcomes and identified some elements of the protocol as being more crucial than others. However, our findings reflect the specific circumstances that prevailed during the study and do not contradict that it may be the combination of each of the different elements that makes an effective regimen rather than the single element on its own. This may also be worth considering when implementing the ERAS protocol in other abdominal surgical procedures.[33,34]

In conclusion, better adherence to the elements of the ERAS protocol is crucial to improve surgical outcome. In this study in particular, restricted perioperative intravenous fluid management and a preoperative carbohydrate drink were found to be of specific importance for beneficial outcomes.

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Online-Only Material: The eTable is available at http://www.archsurg.com.
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REFERENCES

1. Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. The Enhanced Recovery After Surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin Nutr.* 2010;29(4):434-440.
2. Wind J, Polle SW, Fung Kon Jin PH, et al; Laparoscopy and/or Fast Track Multimodal Management Versus Standard Care (LAFA) Study Group; Enhanced Recovery after Surgery (ERAS) Group. Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg.* 2006;93(7):800-809.
3. Kehlet H, Wilmore DW. Evidence-based surgical care and the evolution of fast-track surgery. *Ann Surg.* 2008;248(2):189-198.
4. Eskicioglu C, Forbes SS, Aarts MA, Okrainec A, McLeod RS. Enhanced Recovery After Surgery (ERAS) programs for patients having colorectal surgery: a meta-analysis of randomized trials. *J Gastrointest Surg.* 2009;13(12):2321-2329.
5. Lassen K, Hannemann P, Ljungqvist O, et al; Enhanced Recovery After Surgery Group. Patterns in current perioperative practice: survey of colorectal surgeons in five northern European countries. *BMJ.* 2005;330(7505):1420-1421.
6. Polle SW, Wind J, Fuhring JW, Hofland J, Gouma DJ, Bemelman WA. Implementation of a fast-track perioperative care program: what are the difficulties? *Dig Surg.* 2007;24(6):441-449.
7. Arsalani-Zadeh R, Ullah S, Khan S, Macfie J. Current pattern of perioperative practice in elective colorectal surgery: a questionnaire survey of ACPGBI members. *Int J Surg.* 2010;8(4):294-298.
8. Lloyd GM, Kirby R, Hemingway DM, Keane FB, Miller AS, Neary P. The RAPID protocol enhances patient recovery after both laparoscopic and open colorectal resections. *Surg Endosc.* 2010;24(6):1434-1439.
9. Fearon KC, Ljungqvist O, Von Meyenfeldt M, et al. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. *Clin Nutr.* 2005;24(3):466-477.
10. Lassen K, Soop M, Nygren J, et al; Enhanced Recovery After Surgery (ERAS) Group. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. *Arch Surg.* 2009;144(10):961-969.
11. Maessen J, Dejong CH, Hausel J, et al. A protocol is not enough to implement an enhanced recovery programme for colorectal resection. *Br J Surg.* 2007;94(2):224-231.
12. Nygren J, Thorell A, Jacobsson H, et al. Preoperative gastric emptying: effects of anxiety and oral carbohydrate administration. *Ann Surg.* 1995;222(6):728-734.

13. Olin AO, Osterberg P, Hådell K, Armyr I, Jerström S, Ljungqvist O. Energy-enriched hospital food to improve energy intake in elderly patients. *JPEN J Parenter Enteral Nutr*. 1996;20(2):93-97.
14. Buzby GP, Knox LS, Crosby LO, et al. Study protocol: a randomized clinical trial of total parenteral nutrition in malnourished surgical patients. *Am J Clin Nutr*. 1988;47(2)(suppl):366-381.
15. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. *Am J Surg*. 2002;183(6):630-641.
16. Basse L, Hjort Jakobsen D, Billesbølle P, Werner M, Kehlet H. A clinical pathway to accelerate recovery after colonic resection. *Ann Surg*. 2000;232(1):51-57.
17. Basse L, Raskov HH, Hjort Jakobsen D, et al. Accelerated postoperative recovery programme after colonic resection improves physical performance, pulmonary function and body composition. *Br J Surg*. 2002;89(4):446-453.
18. Basse L, Thorbøl JE, Løssl K, Kehlet H. Colonic surgery with accelerated rehabilitation or conventional care. *Dis Colon Rectum*. 2004;47(3):271-277, discussion 277-278.
19. Stephen AE, Berger DL. Shortened length of stay and hospital cost reduction with implementation of an accelerated clinical care pathway after elective colon resection. *Surgery*. 2003;133(3):277-282.
20. Delaney CP, Fazio VW, Senagore AJ, Robinson B, Halverson AL, Remzi FH. 'Fast track' postoperative management protocol for patients with high comorbidity undergoing complex abdominal and pelvic colorectal surgery. *Br J Surg*. 2001;88(11):1533-1538.
21. Anderson AD, McNaught CE, MacFie J, Tring I, Barker P, Mitchell CJ. Randomized clinical trial of multimodal optimization and standard perioperative surgical care. *Br J Surg*. 2003;90(12):1497-1504.
22. DiFronzo LA, Yamin N, Patel K, O'Connell TX. Benefits of early feeding and early hospital discharge in elderly patients undergoing open colon resection. *J Am Coll Surg*. 2003;197(5):747-752.
23. Schwenk W, Neudecker J, Raue W, Haase O, Müller JM. "Fast-track" rehabilitation after rectal cancer resection. *Int J Colorectal Dis*. 2006;21(6):547-553.
24. Nygren J, Soop M, Thorell A, Hausel J, Ljungqvist O; ERAS Group. An enhanced-recovery protocol improves outcome after colorectal resection already during the first year: a single-center experience in 168 consecutive patients. *Dis Colon Rectum*. 2009;52(5):978-985.
25. Ahmed J, Khan S, Gatt M, Kallam R, MacFie J. Compliance with enhanced recovery programmes in elective colorectal surgery. *Br J Surg*. 2010;97(5):754-758.
26. Soop M, Nygren J, Myrenfors P, Thorell A, Ljungqvist O. Preoperative oral carbohydrate treatment attenuates immediate postoperative insulin resistance. *Am J Physiol Endocrinol Metab*. 2001;280(4):E576-E583.
27. Crowe PJ, Dennison A, Royle GT. The effect of pre-operative glucose loading on postoperative nitrogen metabolism. *Br J Surg*. 1984;71(8):635-637.
28. Yuill KA, Richardson RA, Davidson HI, Garden OJ, Parks RW. The administration of an oral carbohydrate-containing fluid prior to major elective upper-gastrointestinal surgery preserves skeletal muscle mass postoperatively: a randomised clinical trial. *Clin Nutr*. 2005;24(1):32-37.
29. Svanfeldt M, Thorell A, Hausel J, et al. Randomized clinical trial of the effect of preoperative oral carbohydrate treatment on postoperative whole-body protein and glucose kinetics. *Br J Surg*. 2007;94(11):1342-1350.
30. Hausel J, Nygren J, Lagerkranser M, et al. A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients. *Anesth Analg*. 2001;93(5):1344-1350.
31. Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *Lancet*. 2002;359(9320):1812-1818.
32. Brandstrup B, Tønnesen H, Beier-Holgersen R, et al; Danish Study Group on Perioperative Fluid Therapy. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens. a randomized assessor-blinded multicenter trial. *Ann Surg*. 2003;238(5):641-648.
33. Borendal Wodlin N, Nilsson L, Kjølhede P; for the GASPI study group. The impact of mode of anaesthesia on postoperative recovery from fast-track abdominal hysterectomy: a randomised clinical trial [published online September 14, 2010]. *BJOG*. doi:10.1111/j.1471-0528.2010.02697.x.
34. Lassen K, Kjaeve J, Fetveit T, et al. Allowing normal food at will after major upper gastrointestinal surgery does not increase morbidity: a randomized multicenter trial. *Ann Surg*. 2008;247(5):721-729.

INVITED CRITIQUE

Enhanced Recovery Programs

Major Benefits Demonstrated Again

On its face, the ERAS program is a combination of simple, low-risk interventions that, when used in an integrated approach, can reduce LOS and major complications. The benefits have been proven in multiple studies, mostly from Europe, on colorectal surgery patients, not limited to patients with cancer. Gustafsson et al contribute additional information on a large number of patients who underwent resection of colorectal cancers. The data compare an earlier phase (2002-2005) during which ERAS was poorly implemented with a more recent phase (2005-2007) during which more substantial efforts achieved significantly higher compliance with the protocol. Fewer major complications, fewer debilitating postoperative symptoms, and more frequent discharges within LOS targets were seen during the more recent phase of practice and in patients with better compliance with ERAS components. Causality can be questioned since patients who have major complications are ill and less likely to participate in various postoperative ERAS activities such as ambulation and early refeeding. However, multivariable analysis showed 2 early interventions in the process of surgery and recovery to be independent predictors of postoperative outcomes: preoperative carbohydrate loading and perioperative fluid restriction.

The ERAS programs are not known to be widely adopted in the United States. An ERAS program requires a multidisciplinary collaboration between surgeons, anesthesiologists, and nurses. Preoperative carbohydrate loading involves oral intake up until 2 hours prior to induction, which may not be accepted among anesthesiologists. Limiting fluid administration during surgery is also primarily under control of the anesthesiologist. Nearly all ERAS programs include a preoperative education session to promote patient participation in postoperative components of the proto-