Enhanced recovery after surgery (ERAS) protocols: Time to change practice?

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Abstract

Radical cystectomy with pelvic lymph node dissection remains the standard treatment for patients with muscle invasive bladder cancer. Despite improvements in surgical technique, anesthesia and perioperative care, radical cystectomy is still associated with greater morbidity and prolonged in-patient stay after surgery than other urological procedures. Enhanced recovery after surgery (ERAS) protocols are multimodal perioperative care pathways designed to achieve early recovery after surgical procedures by maintaining preoperative organ function and reducing the profound stress response following surgery. The key elements of ERAS protocols include preoperative counselling, optimization of nutrition, standardized analgesic and anesthetic regimens and early mobilization. Despite the significant body of evidence indicating that ERAS protocols lead to improved outcomes, they challenge traditional surgical doctrine, and as a result their implementation has been slow.

The present article discusses particular aspects of ERAS protocols which represent fundamental shifts in surgical practice, including perioperative nutrition, management of postoperative ileus and the use of mechanical bowel preparation.

Introduction

Radical cystectomy with pelvic lymph node dissection remains the standard treatment for patients with muscle invasive bladder cancer.[1] Despite improvements in surgical technique, anesthesia and perioperative care, radical cystectomy is still associated with greater morbidity and prolonged in-patient stay after surgery than other urological procedures. Overall complication rates have been reported as high as 64% at 90 days,[2] with an average in-patient stay of 17.4 days.[3]

Enhanced recovery after surgery (ERAS) protocols are multimodal perioperative care pathways designed to achieve early recovery after surgical procedures by maintaining preoperative organ function and reducing the profound stress response following surgery. The key elements of ERAS protocols include preoperative counselling, optimization of nutrition, standardized analgesic and anesthetic regimens and early mobilization.[4-8] Despite the significant body of evidence indicating that ERAS protocols lead to improved outcomes,[9,10] they challenge traditional surgical doctrine, and as a result their implementation has been slow. Although much of the data arise from colorectal surgery, the evidence is applicable to major urological surgery, in particular radical cystectomy. The present article discusses particular aspects of ERAS protocols which represent fundamental shifts in surgical practice, including perioperative nutrition, management of postoperative ileus and the use of mechanical bowel preparation.

What is ERAS?

Initiated by Professor Henrik Kehlet in the 1990s,[11] ERAS, enhanced recovery programs (ERPs) or "fast-track" programs have become an important focus of perioperative management after colorectal surgery,[12] vascular surgery,[13] thoracic surgery[14] and more recently radical cystectomy.[7,8,15] These programs attempt to modify the physiological and psychological responses to major surgery,[16] and have been shown to lead to a reduction in complications and hospital stay, improvements in cardiopulmonary function, earlier return of bowel function and earlier resumption of normal activities.[9,10] The key principles of the ERAS protocol include preoperative counselling , preoperative nutrition, avoidance of perioperative fasting and carbohydrate loading up to 2 hours preoperatively, standardized anesthetic and analgesic regimens (epidural and non-opiod analgesia) and early mobilization (Fig. 1).[17] There are relatively few reports on the use of ERAS in urological surgery. The introduction of ERAS in a centre in the United Kingdom lead to a significant reduction

in hospital stay and equivalent morbidity in radical cystectomy patients, compared to traditional approaches.[7,15] The protocol focused on reduced bowel preparation, standardized feeding schedule and standardized analgesic regimens (Table 1). Similar findings have been replicated in a small number of other urological publications.[18,19]

Perioperative nutrition

Preoperative nutrition

It is well-known that poor nutrition is detrimental to outcomes postoperatively.[20,21] It frequently occurs with comorbidities and with underlying disease processes, such as cancer.[22] Inadequate nutrition, particularly for cancer patients undergoing surgery, is an independent risk factor for complications, increased hospital stay and costs.[23] The importance of nutritional status in patients undergoing radical cystectomy has long been noted,[24] with reported complications rates as high as 80% in patients with poor nutrition.[25] More recently, data from Vanderbilt University demonstrate that nutritional deficiency preoperatively is a strong predictor of 90-day mortality and poor overall survival.[26] It is therefore unsurprising that assessment and treatment of poor nutrition is an essential component of ERAS protocols. In terms of defining the problem, the European Society of Parenteral and Enteral Nutrition (ESPEN) defines "severe" nutritional risk as one or more of the following: weight loss >10% to 15% in 6 months, body mass index <18.5 kg/m2 or a serum albumin of <30 g/L.[17] The British Association of Parenteral and Enteral uses similar parameters as part of the Malnutrition Universal Screening Tool (MUST) to risk stratify patients according to their nutritional level. What is interesting when considering the patients who undergo radical cystectomy is how many would be classified as high risk or severe nutritional risk after appropriate assessment. Correction of preoperative nutritional deficiencies may sometimes require prolonged parenteral, or a combination of parenteral and enteral nutrition depending on the severity of the problem and the patient's gastrointestinal function. However, in most cases patients can be managed with appropriate input from a dietician or nutritionist, and the use of a standard whole protein liquid nutritional supplement.

Carbohydrate loading and early enteral feeding

The stress response is initiated by a variety of physical insults, such as tissue injury, infection, hypovolemia or hypoxia. The ERAS program is aimed at attenuating the body's response to surgery which is characterized by its catabolic effect.[27] Autonomic afferent impulses from the area of injury or trauma stimulate the hypothalamus-pituitary-adrenal axis and mediate the body's subsequent endocrine response.[28] Increased cortisol levels stimulate gluconeogenesis and glyconeogenesis in the liver, with triglycerides

Table 1. An enhanced recovery after surgery for radical cystectomy ± neobladder focusing on reduced bowel preparation and standardized feeding and analgesic regimens

Day before radical cystectomy - Normal breakfast - Admit to hospital - Unrestricted clear fluids - Refer to dietician - Stoma therapist to see patient - Assess social circumstances and refer if needed	**Day 3 and 4** - Remove epidural on day 3 - Continue to mobilize and encourage self-care - Light diet as tolerated - Start planning for discharge
Day of radical cystectomy - Clear carbohydrate drinks up to 2 hours before surgery, then nil by mouth - Restart clear fluids as tolerated when in recovery - Start food chart - Epidural analgesia in situ	**Day 5, 6 and 7** - Dietician to assess nutritional requirements on day 5 - If a patient is not eating or drinking after 5 to 6 days, but with bowel activity, then start nasogastric feeding - If there is no bowel activity then start total parenteral nutrition
After radical cystectomy: Day 1 - Free fluids as tolerated - Female patients, remove vaginal pack - Mobilize and refer to physiotherapist - Ranitidine 3 times daily intravenously or twice daily orally - Remove drain if draining <50 mL in 24 hours - Flush 20 mL into neobladder, twice hourly for 12 hours and then 4 times hourly	**Day 8** - Stents out (no stentogram) **Day 10** - Remove clips
Day 2 - Light diet as tolerated - Mobilize and encourage self-care (catheter care/flushing in neobladders, and stoma bag emptying in patients with a conduit)	**Day 11 to 14** - Continue as previous and schedule for return to home

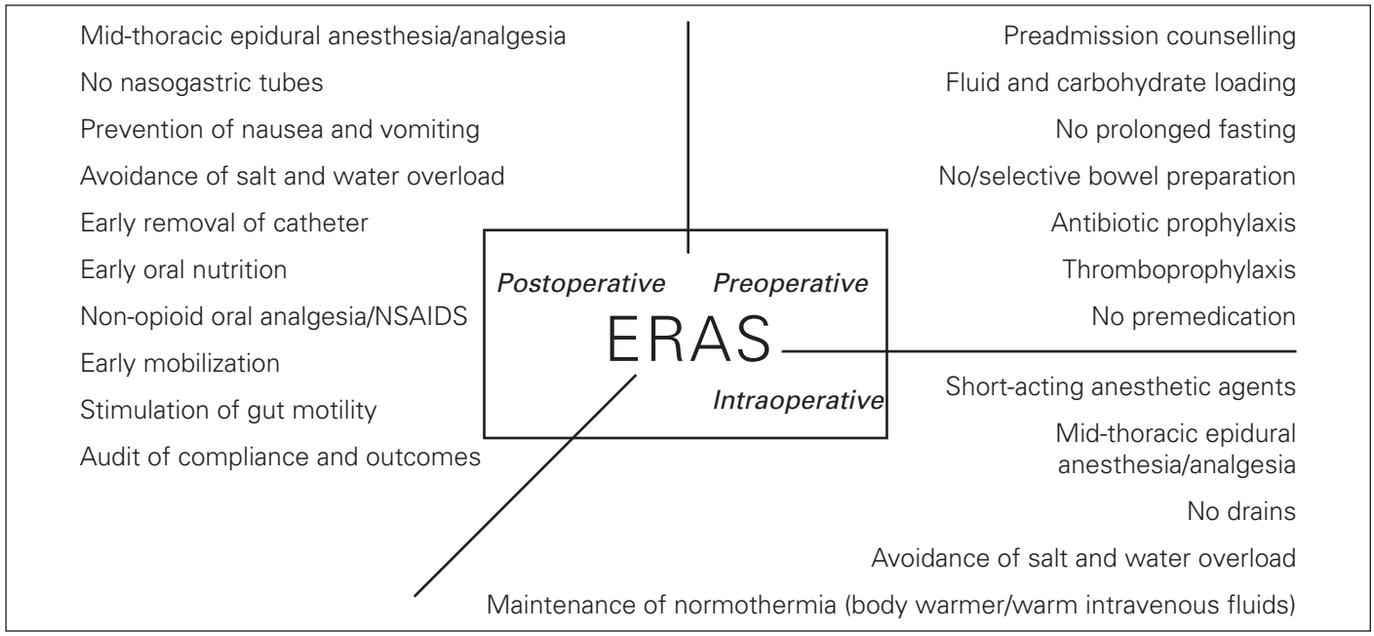

Fig. 1. Key aspects of ERAS protocols. Adapted from Donat et al. Early nasogastric tube removal combined with metoclopramide after radical cystectomy and urinary diversion. *J Urol* 1999;162:1599-602.[70]

being converted to glycerol and fatty acids providing the substrates for gluconeogensis. Adrenocorticotropic hormone and cortisol production leads to protein catabolism, weight loss, muscle (skeletal and visceral) wasting and nitrogenous loss.[27] There is also a relative lack of insulin and peripheral insulin resistance occurs due to alpha-2-adrenergic inhibition of pancreatic B cells (facilitated by catecholamines) and defects in the insulin receptor/intracellular signalling pathway. Hyperglycaemia is therefore a significant finding after cystectomy,[29] and the observed insulin resistance is a major variable influencing length of stay,[30] poor wound healing and increased risk of infective complications. The degree of insulin resistance is associated with the extent of surgery, and if postoperative hyperglycaemia is controlled, mortality and morbidity can be reduced by half.[31] Methods which reduce the insulin resistance include adequate pain relief,[32,33] avoiding a prolonged period when oral intake is interrupted, and the use of carbohydrate loading.

The practice of fasting patients from midnight is used to avoid pulmonary aspiration after elective surgery; however, there is no evidence to support this.[34] Preoperative fasting actually increases the metabolic stress, hyperglycemia and insulin resistance, which the body is already prone to during the surgical process.[30] Changing the metabolic state of patients by shortening preoperative fasting not only decreases insulin resistance, but reduces protein loss and improves muscle function.[35] A review of 22 RCTs comparing different perioperative fasting regimens and perioperative complications revealed that there is no evidence to suggest a shortened fluid fast results in an increased risk of aspiration, regurgitation or related morbidity compared to the standard fasting from midnight policy.[36] Furthermore, if patients are allowed to take solids up to 6 hours preoperatively and clear fluids up to 2 hours, there is no increase in complications,[36,37] which forms the basis of preoperative guidelines adopted by the Royal College of Anaesthetists[38] and the American Society of Anesthesiologists.[39]

As mentioned previously, the use of carbohydrate loading attenuates postoperative insulin resistance, reduces nitrogen and protein losses,[40,41] preserves skeletal muscle mass and reduces preoperative thirst, hunger and anxiety.[42-44] It involves the use of clear carbohydrate drinks the day prior to surgery and up to 2 hours before. In addition to the metabolic effects, it facilitates accelerated recovery through early return of bowel function and shorter hospital stay, ultimately leading to an improved perioperative well-being.[45-47] As a result, it is an important element of the nutritional aspects of ERAS and should replace the practice of overnight fasting.

Role of mechanical bowel preparation

The routine use of preoperative mechanical bowel preparation (MBP) has long been a tradition in colorectal surgery; due to the use of bowel segments, MBP is used routinely for radical cystectomy patients. The aim of MBP is to rid the large bowel of solid fecal contents and to lower the bacterial load, thereby reducing the incidence of postoperative complications. However, MBP liquefies solid faeces, which may increase the risk of intra-operative spillage of contaminant, and it is almost impossible to reduce the bacterial load in the

bowel due to the vast number of micro-organisms present in the digestive tract.[48]

The routine practice of MBP has been challenged for over 30 years. In 1972, Hughes originally questioned MBP and concluded that vigorous mechanical bowel preparation is unnecessary.[49] Not only does MBP cause metabolic and electrolyte imbalance, dehydration, abdominal pain/bloating and fatique,[50-53] but it may actually have detrimental effects on surgical outcome.[54] Multiple RCTs and meta-analyses have been published over the last decade suggesting that it is safe to abandon MBP.[54-59] One of the largest RCTs from Denmark was published in 2007.[60] The primary objective was to assess the outcome of elective colorectal resections with or without MBP. The authors examined 1431 patients at 13 colorectal centres and found no difference in anastamotic leakage, septic complications, fascial dehiscence or mortality between the groups. In addition to an absence of benefit, MBP is also likely associated with an increased risk of complications, particularly anastamostic leakage.[59] A meta-analysis of 10 trials and nearly 2000 patients published in 2007, not only found an increased incidence of anastamotic leaks and wound infections, but also a trend toward increased incidence of intra-abdominal abscesses and extradigestive complications.[54] With this in mind, Slim and colleagues published an updated meta-analysis and review of the literature which included 14 RCTs and nearly 5000 patients.[61] Although it did not confirm the harmful effect of MBP as previously suggested, it demonstrated that any kind of MBP can safely be omitted before colonic surgery.

In terms of radical cystectomy, Shafii and colleagues conducted a retrospective study assessing no bowel preparation versus bowel preparation before cystectomy and urinary diversion. They authors concluded that in the group who received MBP, there was a higher incidence postoperative ileus, slower commencement of diet, greater risk of wound dehiscence and longer hospital stay (31.6 vs. 22.8 days) compared to the group who did not receive MBP.[62]

Postoperative nutrition

In addition to preoperative carbohydrate loading, early postoperative nutrition can ameliorate the metabolic response leading to less insulin resistance, lower nitrogen losses and reduce the loss of muscle strength.[63,64] An assessment of gastrointestinal function and patient tolerability is essential when commencing postoperative oral intake. Multiple studies exist on the timing of post-operative nutrition. One of the early meta-analyses, although relatively small, found that there is no advantage in keeping patients nil by mouth after elective gastrointestinal resection and early feeding may actually be beneficial by reducing infectious complications and length of hospital stay.[63] Lewis and colleagues demonstrated no detrimental effect with early feeding, but a trend towards a lower incidence of anastomotic dehiscence, wound infection, pneumonia, intra-abdominal abscess or mortality in patients who received early enteral feeding. A Cochrane review in 2006 found a direction of effect towards a reduction in complications and mortality rate,[65] and in an update to their original metanalysis, Lewis and colleagues confirmed no benefit to keeping patients nothing by mouth (NBM) postoperatively, a reduction in complications and a reduced mortality rate; although, the mechanism for reduced mortality remains unclear.[66]

Prevention of prolonged postoperative ileus

Bowel complications, and particularly paralytic ileus, are among the most common problems following radical cystectomy.[3,7,67,68] The etiology of postoperative ileus is multifactoral, with bowel function relying on a combination of the enteric and central nervous systems, hormonal influences, neurotransmitters and local inflammatory pathways.[69] Surgical stress, bowel handling, opioids and intraoperative fluid resuscitation can disrupt these normal arrangements within the gastrointestinal tract and lead to postoperative ileus and impaired gastrointestinal absorptive function.[64] Factors that help reduce this include epidural anesthesia, minimally invasive surgery, gentle tissue handling, avoiding of fluid overload[70] and early feeding.[18,71] Furthermore, the use of routine nasogastric decompression should be avoided after surgery as the incidence of fever, atelectasis and pneumoniae are increased in patients with nasogastric tube drainage, and any nasogastric tubes placed during surgery should be removed prior to extubation.[10,72]

Chewing gum has previously been used in an attempt to improve the postoperative recovery of bowel function in patients. Chewing gum in the postoperative period has been described as a form of sham feeding,[73] whereby a food substance is chewed but does not enter the stomach. Gum is postulated to increase cephalo-vagal stimulation, leading to increased gastric motility and reduced inhibitory inputs from the sympathetic nervous system. Gastrointestinal hormones, such as gastrin, neurotensin, cholecystokinin and pancreatic polypeptide, are also increased and result in vagal stimulation of smooth muscle fibres.[74] Chewing gum also increases secretion of saliva and pancreatic juices, and a recent study proposed that sorbitol and hexitol found in sugar-free gum may also play a role in the reduction of postoperative ileus.[75] A number of studies exist which demonstrate the benefits in patients undergoing colorectal surgery.[73,74,76-78] A meta-analysis of several RCTs evaluating the effect of chewing gum on postoperative ileus has subsequently been published. Although there are relatively low patient numbers and a significant heterogeneity of studies, chewing gum offers significant benefits by reducing the time to pass flatus and the time until first bowel movement.[79-82]

The use of bowel segments in the reconstruction of the urinary tract after cystectomy lead Kouba and colleagues to examine the use of chewing gum following cystectomy.[83] The time to flatus was shorter in patients who received gum compared with controls (2.4 vs. 2.9 days). Also, time to bowel movement was reduced in patients who received gum (3.2 vs. 3.9 days). There was no significant difference in length of hospital stay between gum-chewing patients and controls (4.7 vs. 5.1 days). A similar picture was noted by Koupparis and colleagues who examined the addition of chewing gum postoperatively to their established enhanced recovery program.[15] The authors noted a significant reduction in the duration of postoperative ileus, but with only a trend towards a reduced in-patient stay.

Health economic benefits

The implementation of ERAS protocols represents a significant change in practice and a potential increase in the use of resources. Certain aspects, such as chewing gum, represent a simple and cheap intervention, which could potentially lead to significant cost savings. Schuster and colleagues estimated that the use of chewing gum following colectomy could save $118 828 000 per year in the United States.[76] However, few studies have examined the impact of introducing an ERAS program on quality of life or health economic outcomes in the months after surgery. The benefits of ERAS will be markedly reduced if the costs are simply transferred to the community or if patients suffer a greater deterioration in quality of life than is experienced with conventional care. King and colleagues examined information regarding in-patient days, out-patient and general practitioner visits and the use of community services and estimated costs from national published figures.[84] Direct medical and indirect non-medical costs were significantly lower in the ERAS group. Similarly, Sammour and colleagues have recently published a cost-analysis of ERAS in colorectal surgery.[85] They evaluated whether costs saved by reduced postoperative resource utilization would offset the financial burden of setting up and maintaining such an ERAS program. There was a significant reduction in total hospital stay, intravenous fluid use, complications and duration of epidural use in the ERAS group. The implementation of an ERAS program costs about $102 000, but this was offset by costs saved in reduced postoperative resource utilization, with an overall cost-saving of roughly $6900 per patient.

An ongoing trial is the Tapas-study. It was conceived to determine which of the three treatment programs (open conventional surgery, open "ERAS" surgery or laparoscopic "ERAS" surgery for patients with colon carcinomas) is the most cost-effective.[86] Primary outcome parameters are direct medical costs and indirect non-medical costs, with the aim of directing future investment appropriately.

Conclusions

Enhanced recovery after surgery protocols were initially described in open colorectal surgery, but have since been studied in a variety of surgical specialties, including urology. Although growing evidence from several RCTs, systematic reviews and meta-analyses suggest significant benefits from ERAS pathways, there are still major difficulties when introducing these evidence-based guidelines into routine practice.[9,84,87] The fact that less than half of patients are involved in a postoperative care pathway suggests that perioperative care continues to resemble traditional and conventional attitudes.[88,89] Many surgeons state that they have "never heard of ERAS," while others cite inadequate multidisciplinary and community support as an impediment to implementation.[90]

In terms of barriers to introducing ERAS, even the simple measures discussed in this review still represent fundamental changes in practice, and can therefore be difficult to achieve. Kahokher and colleagues outlined the key aspects required for the implementation of an ERAS protocol.[91] One of the most important aspects is the ERAS team, which includes pre-admission staff, dieticians, nurses, physiotherapists, social workers, occupational therapists and doctors. All team members must be familiar ERAS principles and be motivated to carry out the program; they must be able to overcome traditional concepts, teaching and attitudes towards perioperative care. In light of such compelling evidence, the evidence-based environment in which we practice demands that we review the perioperative management of radical cystectomy patients and alter it accordingly.

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This paper has been peer-reviewed.

References

1. Ghoneim MA, el-Mekresh MM, el-Baz MA, el-Attar IA, Ashamallah A. Radical cystectomy for carcinoma of the bladder: critical evaluation of the results in 1,026 cases. *J Urol* 1997;158:393-9.
2. Shabsigh A, Korets R, Vora KC, et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. *Eur Urol* 2009;55:164-74.
3. Novotny V, Hakenberg OW, Wiessner D, et al. Perioperative complications of radical cystectomy in a contemporary series. *Eur Urol* 2007;51:397-401; discussion 01-2.
4. Wilmore DW, Kehlet H. Management of patients in fast track surgery. *BMJ* 2001;322:473-6.
5. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. *Am J Surg* 2002;183:630-41.
6. Kehlet H, Dahl JB. Anaesthesia, surgery, and challenges in postoperative recovery. *Lancet* 2003;362:1921-8.
7. Arumainayagam N, McGrath J, Jefferson KP, et al. Introduction of an enhanced recovery protocol for radical cystectomy. *BJU Int* 2008;101:698-701.
8. Kehlet H, Mogensen T. Hospital stay of 2 days after open sigmoidectomy with a multimodal rehabilitation programme. *Br J Surg* 1999;86:227-30.
9. Eskicioglu C, Forbes SS, Aarts MA, et al. Enhanced recovery after surgery (ERAS) programs for patients having colorectal surgery: a meta-analysis of randomized trials. *J Gastrointest Surg* 2009;13:2321-9.
10. Lassen K, Soop M, Nygren J, et al. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. *Arch Surg* 2009;144:961-9.

11. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br J Anaesth* 1997;78:606-17.
12. Wind J, Polle SW, Fung Kon Jin PH, et al. Systematic review of enhanced recovery programmes in colonic surgery. *Br J Surg* 2006;93:800-9.
13. Podore PC, Throop EB. Infrarenal aortic surgery with a 3-day hospital stay: A report on success with a clinical pathway. *J Vasc Surg* 1999;29:787-92.
14. Tovar EA, Roethe RA, Weissig MD, et al. One-day admission for lung lobectomy: an incidental result of a clinical pathway. *Ann Thorac Surg* 1998;65:803-6.
15. Koupparis A, Dunn J, Gillatt D, et al. Improvement of an enhanced recovery protocol for radical cystecomy. *British Journal of Medical and Surgical Urology* 2010;3:237-40.
16. 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;24:466-77.
17. Weimann A, Braga M, Harsanyi L, et al. ESPEN Guidelines on Enteral Nutrition: Surgery including organ transplantation. *Clin Nutr* 2006;25:224-44.
18. Pruthi RS, Chun J, Richman M. Reducing time to oral diet and hospital discharge in patients undergoing radical cystectomy using a perioperative care plan. *Urology* 2003;62:661-5; discussion 65-6.
19. Pruthi RS, Nielsen M, Smith A, et al. Fast track program in patients undergoing radical cystectomy: results in 362 consecutive patients. *J Am Coll Surg* 2010;210:93-9.
20. Durkin MT, Mercer KG, McNulty MF, et al. Vascular surgical society of great britain and ireland: contribution of malnutrition to postoperative morbidity in vascular surgical patients. *Br J Surg* 1999;86:702.
21. van Bokhorst-de van der Schueren MA, van Leeuwen PA, Sauerwein HP, et al. Assessment of malnutrition parameters in head and neck cancer and their relation to postoperative complications. *Head Neck* 1997;19:419-25.
22. Von Meyenfeldt MF, Meijerink WJ, Rouflart MM, et al. Perioperative nutritional support: a randomised clinical trial. *Clin Nutr* 1992;11:180-6.
23. Correia MI, Caiaffa WT, da Silva AL, et al. Risk factors for malnutrition in patients undergoing gastroenterological and hernia surgery: an analysis of 374 patients. *Nutr Hosp* 2001;16:59-64.
24. Mohler JL, Flanigan RC. The effect of nutritional status and support on morbidity and mortality of bladder cancer patients treated by radical cystectomy. *J Urol* 1987;137:404-7.
25. Herranz Amo F, Garcia Peris P, Jara Rascon J, et al. [Usefulness++ of total parenteral nutrition in radical surgery for bladder cancer]. *Actas Urol Esp* 1991;15:429-36.
26. Gregg JR, Cookson MS, Phillips S, et al. Effect of preoperative nutritional deficiency on mortality after radical cystectomy for bladder cancer. *J Urol* 2011;185:90-6.
27. Desborough JP. The stress response to trauma and surgery. *Br J Anaesth* 2000;85:109-17.
28. Hall GM. The anaesthetic modffication of the endocrine and metabolic response to surgery. *The Annals of The Royal College of Surgeons of England* 1985;67:25-29.
29. Mathur S, Plank LD, Hill AG, et al. Changes in body composition, muscle function and energy expenditure after radical cystectomy. *BJU Int* 2008;101:973-7; discussion 77.
30. Thorell A, Nygren J, Ljungqvist O. Insulin resistance: a marker of surgical stress. *Curr Opin Clin Nutr Metab Care* 1999;2:69-78.
31. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. *N Engl J Med* 2001;345:1359-67.
32. Greisen J, Juhl CB, Grofte T, et al. Acute pain induces insulin resistance in humans. *Anesthesiology* 2001;95:578-84.
33. Uchida I, Asoh T, Shirasaka C, et al. Effect of epidural analgesia on postoperative insulin resistance as evaluated by insulin clamp technique. *Br J Surg* 1988;75:557-62.
34. Crowe PJ, Dennison A, Royle GT. The effect of pre-operative glucose loading on postoperative nitrogen metabolism. *Br J Surg* 1984;71:635-7.
35. Ljungqvist O, Soreide E. Preoperative fasting. *Br J Surg* 2003;90:400-6.
36. Brady M, Kinn S, Stuart P. Preoperative fasting for adults to prevent perioperative complications. *Cochrane Database Syst Rev* 2003:CD004423.
37. Brady M, Kinn S, O'Rourke K, et al. Preoperative fasting for preventing perioperative complications in children. *Cochrane Database Syst Rev* 2005:CD005285.
38. Anaesthetists TRCo. *Guidance on the provision of anaesthesia services for Pre-operative Care*, 2009.
39. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: a report by the American Society of Anesthesiologist Task Force on Preoperative Fasting. *Anesthesiology* 1999;90:896-905.
40. 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;94:1342-50.
41. Soop M, Carlson GL, Hopkinson J, et al. Randomized clinical trial of the effects of immediate enteral nutrition on metabolic responses to major colorectal surgery in an enhanced recovery protocol. *Br J Surg* 2004;91:1138-45.
42. Nygren J, Soop M, Thorell A, et al. Preoperative oral carbohydrate administration reduces postoperative insulin resistance. *Clin Nutr* 1998;17:65-71.
43. Soop M, Nygren J, Thorell A, et al. Preoperative oral carbohydrate treatment attenuates endogenous glucose release 3 days after surgery. *Clin Nutr* 2004;23:733-41.
44. Soop M, Myrenfors P, Nygren J, et al. Preoperative oral carbohydrate intake attenuates metabolic changes immediately after hip replacement. *Clinical Nutrition* 1998;17(Supp 1):3-4.
45. Nygren J, Thorell A, Ljungqvist O. Preoperative oral carbohydrate nutrition: an update. *Curr Opin Clin Nutr Metab Care* 2001;4:255-9.
46. Hausel J, Nygren J, Lagerkranser M, et al. A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients. *Anesth Analg* 2001;93:1344-50.
47. Noblett SE, Watson DS, Huong H, et al. Pre-operative oral carbohydrate loading in colorectal surgery: a randomized controlled trial. *Colorectal Dis* 2006;8:563-9.
48. Mahajna A, Krausz M, Rosin D, et al. Bowel preparation is associated with spillage of bowel contents in colorectal surgery. *Dis Colon Rectum* 2005;48:1626-31.
49. Hughes ES. Asepsis in large-bowel surgery. *Ann R Coll Surg Engl* 1972;51:347-56.
50. Beloosesky Y, Grinblat J, Weiss A, et al. Electrolyte disorders following oral sodium phosphate administration for bowel cleansing in elderly patients. *Arch Intern Med* 2003;163:803-8.
51. Frizelle FA, Colls BM. Hyponatremia and seizures after bowel preparation: report of three cases. *Dis Colon Rectum* 2005;48:393-6.
52. Beck DE. Mechanical bowel cleansing for surgery. *Perspect Colon Rectal Surg* 1994;7:97-114.
53. Kim HJ, Yoon YM, Park KN. The changes in electrolytes and acid-base balance after artificially induced acute diarrhea by laxatives. *J Korean Med Sci* 1994;9:388-93.
54. Bucher P, Mermillod B, Gervaz P, et al. Mechanical bowel preparation for elective colorectal surgery: a meta-analysis. *Arch Surg* 2004;139:1359-64; discussion 65.
55. Brownson P, Jenkins SA, Nott D. Mechanical bowel preparation before colorectal surgery: results of a prospective randomized trial. *Br J Surg* 1992;79:461-2.
56. Santos JC Jr, Batista J, Sirimarco MT, et al. Prospective randomized trial of mechanical bowel preparation in patients undergoing elective colorectal surgery. *Br J Surg* 1994;81:1673-6.
57. Miettinen RP, Laitinen ST, Makela JT, et al. Bowel preparation with oral polyethylene glycol electrolyte solution vs. no preparation in elective open colorectal surgery: prospective, randomized study. *Dis Colon Rectum* 2000;43:669-75; discussion 75-7.
58. Zmora O, Mahajna A, Bar-Zakai B, et al. Colon and rectal surgery without mechanical bowel preparation: a randomized prospective trial. *Ann Surg* 2003;237:363-7.
59. Bucher P, Gervaz P, Soravia C, et al. Randomized clinical trial of mechanical bowel preparation versus no preparation before elective left-sided colorectal surgery. *Br J Surg* 2005;92:409-14.
60. Contant CM, Hop WC, van't Sant HP, et al. Mechanical bowel preparation for elective colorectal surgery: a multicentre randomised trial. *Lancet* 2007;370:2112-7.
61. Slim K, Vicaut E, Launay-Savary M-V, et al. Updated Systematic Review and Meta-Analysis of Randomized Clinical Trials on the Role of Mechanical Bowel Preparation Before Colorectal Surgery. *Ann Surg* 2009;249:203-9.
62. Shafii M, Murphy DM, Donovan MG, et al. Is mechanical bowel preparation necessary in patients undergoing cystectomy and urinary diversion? *BJU Int* 2002;89:879-81.
63. Lewis SJ, Egger M, Sylvester PA, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. *BMJ* 2001;323:773-6.
64. Correia MI, da Silva RG. The impact of early nutrition on metabolic response and postoperative ileus. *Curr Opin Clin Nutr Metab Care* 2004;7:577-83.
65. Andersen HK, Lewis SJ, Thomas S. Early enteral nutrition within 24h of colorectal surgery versus later commencement of feeding for postoperative complications. *Cochrane Database Syst Rev* 2006:CD004080.
66. Lewis SJ, Andersen HK, Thomas S. Early enteral nutrition within 24 h of intestinal surgery versus later commencement of feeding: a systematic review and meta-analysis. *J Gastrointest Surg* 2009;13:569-75.
67. Resnick J, Greenwald DA, Brandt LJ. Delayed gastric emptying and postoperative ileus after nongastric abdominal surgery: part II. *Am J Gastroenterol* 1997;92:934-40.
68. Resnick J, Greenwald DA, Brandt LJ. Delayed gastric emptying and postoperative ileus after nongastric abdominal surgery: part I. *Am J Gastroenterol* 1997;92:751-62.
69. Luckey A, Livingston E, Tache Y. Mechanisms and treatment of postoperative ileus. *Arch Surg* 2003;138:206-14.
70. Varadhan KK, Lobo DN, Ljungqvist O. Enhanced recovery after surgery: the future of improving surgical care. *Crit Care Clin* 2010;26:527-47, x.
71. Donat SM, Slaton JW, Pisters LL, et al. Early nasogastric tube removal combined with metoclopramide after radical cystectomy and urinary diversion. *J Urol* 1999;162:1599-602.
72. Inman BA, Harel F, Tiguert R, et al. Routine nasogastric tubes are not required following cystectomy with urinary diversion: a comparative analysis of 430 patients. *J Urol* 2003;170:1888-91.

73. Asao T, Kuwano H, Nakamura J, et al. Gum chewing enhances early recovery from postoperative ileus after laparoscopic colectomy. *J Am Coll Surg* 2002;195:30-2.
74. Quah HM, Samad A, Neathey AJ, et al. Does gum chewing reduce postoperative ileus following open colectomy for left-sided colon and rectal cancer? A prospective randomized controlled trial. *Colorectal Dis* 2006;8:64-70.
75. Tandeter H. Hypothesis: hexitols in chewing gum may play a role in reducing postoperative ileus. *Med Hypotheses* 2009;72:39-40.
76. Schuster R, Grewal N, Greaney GC, et al. Gum chewing reduces ileus after elective open sigmoid colectomy. *Arch Surg* 2006;141:174-6.
77. Matros E, Rocha F, Zinner M, et al. Does gum chewing ameliorate postoperative ileus? Results of a prospective, randomized, placebo-controlled trial. *J Am Coll Surg* 2006;202:773-8.
78. Hirayama I, Suzuki M, Ide M, et al. Gum-chewing stimulates bowel motility after surgery for colorectal cancer. *Hepatogastroenterology* 2006;53:206-8.
79. Purkayastha S, Tilney HS, Darzi AW, et al. Meta-analysis of randomized studies evaluating chewing gum to enhance postoperative recovery following colectomy. *Arch Surg* 2008;143:788-93.
80. Fitzgerald JE, Ahmed I. Systematic review and meta-analysis of chewing-gum therapy in the reduction of postoperative paralytic ileus following gastrointestinal surgery. *World J Surg* 2009;33:2557-66.
81. Noble EJ, Harris R, Hosie KB, et al. Gum chewing reduces postoperative ileus? A systematic review and meta-analysis. *Int J Surg* 2009;7:100-5.
82. Parnaby CN, MacDonald AJ, Jenkins JT. Sham feed or sham? A meta-analysis of randomized clinical trials assessing the effect of gum chewing on gut function after elective colorectal surgery. *Int J Colorectal Dis* 2009;24:585-92.
83. Kouba EJ, Wallen EM, Pruthi RS. Gum chewing stimulates bowel motility in patients undergoing radical cystectomy with urinary diversion. *Urology* 2007;70:1053-6.
84. King PM, Blazeby JM, Ewings P, et al. Randomized clinical trial comparing laparoscopic and open surgery for colorectal cancer within an enhanced recovery programme. *Br J Surg* 2006;93:300-8.
85. Sammour T, Zargar-Shoshtari K, Bhat A, et al. A programme of Enhanced Recovery After Surgery (ERAS) is a cost-effective intervention in elective colonic surgery. *N Z Med J* 2010;123:61-70.
86. Reurings JC, Spanjersberg WR, Oostvogel HJ, et al. A prospective cohort study to investigate cost-minimisation, of Traditional open, open fAst track recovery and laParoscopic fASt track multimodal management, for surgical patients with colon carcinomas (TAPAS study). *BMC Surg* 2010;10:18.
87. Gouvas N, Tan E, Windsor A, et al. Fast-track vs standard care in colorectal surgery: a meta-analysis update. *Int J Colorectal Dis* 2009;24:1119-31.
88. Polle SW, Wind J, Fuhring JW, et al. Implementation of a fast-track perioperative care program: what are the difficulties? *Dig Surg* 2007;24:441-9.
89. 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;94:224-31.
90. Walter CJ, Smith A, Guillou P. Perceptions of the application of fast-track surgical principles by general surgeons. *Ann R Coll Surg Engl* 2006;88:191-5.
91. Kahokehr A, Sammour T, Zargar-Shoshtari K, et al. Implementation of ERAS and how to overcome the barriers. *Int J Surg* 2009;7:16-9.

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