Review Article



# Enhanced recovery after surgery in urology

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**Abstract:** Major urologic surgery has an association with frequent morbidity and protracted inpatient admissions, especially prolonged surgery such as radical cystectomy (RC). Enhanced recovery after surgery (ERAS) principles originally developed for colorectal surgery have demonstrated reduced surgical stress leading to improved postoperative recovery and reduced length of stay (LOS). This has led to ERAS protocols being adopted across surgical specialities, including urology. ERAS guidelines for urology published in 2013 have since led to extensive research in the implementation of these principles into practice, alongside comparative research into individual ERAS principles such as minimally invasive surgery. Through this review we will demonstrate current evidence and recommendations with consideration of the preoperative, intraoperative and postoperative care, noting areas where evidence is lacking or requires further exploration. We will explore the developments to the implementation of ERAS principles in current practice, including the use of alvimopan to decrease time to first bowel function, the changing role of regional anaesthesia (including the use of locoregional blocks), and the increasing use of minimally invasive surgical technique (e.g., robot assisted RC) leading to overall improved patient care and reduced LOS.

**Keywords:** Minimally invasive surgical procedures; anesthesia recovery period; urinary bladder diseases

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## Introduction

Enhanced recovery after surgery (ERAS) protocols aim to reduce surgical stress and thus improve postoperative recovery and reduce length of stay (LOS) (1). Protocols were originally designed for colorectal surgery, leading to a reduction in complications by 50% and hospital stay by 2.5 days (2). ERAS principles have since been employed in other surgical specialties leading to improved patient outcomes (3), and ERAS programs within urology are predominantly adapted from colorectal protocols (4).

To date ERAS principles have been mainly focussed on radical cystectomy (RC) when employed in urologic surgery, due to the high morbidity, complication rate and prolonged LOS associated with the procedure (5,6). The morbidity can be as significant as 30-64% of patients after open RC with bilateral lymph node dissection, urinary diversion or bladder reconstruction (7).

Following published guidelines for RC in 2013 (8) by the ERAS society protocol development has been slow, but increasingly evidence supporting the use of ERAS in RC has emerged (9-12). In one prospective study Pang *et al.* (9) reported a LOS reduction from 18 to 8 days across 453 patients in their institution once ERAS principles were instigated, along with reduced blood loss and lower re-admission rates. Similar results have been described in other prospective centres internationally, with LOS reductions from 7 to 6 days (10), urinary tract infection rates falling from 10% to 1% (11), LOS reducing despite aging populations during ERAS implementation (12). A recent review of all literature for ERAS in RC identified reduced morbidity, quicker bowel recovery and a reduced LOS than patients treated without ERAS protocolised care, with no

increase in mortality (13).

Several studies have also looked at ERAS for radical prostate surgery (14) and nephrectomy (15) but RC will be the focus of this review.

This article is designed to aid the reader to implement ERAS in major urologic surgery with current evidence. To implement ERAS principles successfully the preoperative, intraoperative and postoperative elements must be considered. A summary of these elements is demonstrated in *Table 1*, and is the structure employed in our centre.

## Pre-operative considerations

### *Patient counselling and education*

Pre-admission counselling and education of anaesthetic and surgical procedures have been shown to reduce anxiety in abdominal surgery (16), enhancing wound healing and post-operative recovery leading to fewer complications. This should include stoma education for patients undergoing ostomy formation, as it is an independent risk factor for delayed discharge (17).

Multi-disciplinary team (MDT) counselling has been component of ERAS implementation by Pang *et al.* (9), involving the surgeon, cancer nurse specialist and stoma therapist in the pre-operative patient education.

### *Medical optimisation*

Pre-operative conditioning measures are outlined within ERAS in rectal and pelvic surgery (18), and include optimisation of common co-morbidities such as hypertension, diabetes and anaemia, alongside encouraging physical exercise and cessation of alcohol and drug abuse and smoking. A minimum 4-week period of abstinence should be recommended to patients before surgery for smokers (8,13), however this period is extended to 8 weeks to accommodate for pulmonary complications that can occur following abrupt smoking cessation in long term smokers (19).

Emphasis should be placed on the nutritional status of the pre-operative patient, as a third of patients are at risk of malnutrition in the perioperative period (20). Standardised nutritional screening can be performed using the Nutritional Risk Score (21), evaluating weight loss, food intake and body mass index, alongside disease severity. Pre-operative immunonutrition (fish oils, nucleotides and arginine) has been implicated in reducing LOS and wound infection risk, possibly through improved immunosuppressive and inflammatory responses post-surgically (22).

### *Bowel preparation*

A systematic review of oral bowel preparation in colorectal surgery identified no advantage to the use of bowel preparation and suggested a higher incidence of anastomotic leakage (23). Xu *et al.* found no benefit from bowel preparation in a randomised controlled trial (RCT) of patients undergoing RC (24). Omitting bowel preparation possibly prevents dehydration, electrolyte imbalance and post-operative ileus.

### *Carbohydrate loading*

Awad *et al.* in their meta-analysis demonstrated a reduction in LOS in patients who have received carbohydrate loading in elective surgery (25). Colorectal ERAS guidelines further demonstrate reduced thirst, insulin resistance and the maintenance of lean body mass including muscle strength following surgery (16).

### *Fasting*

European guidelines, which are now well established, recommend 6-hour fasting for solid food and 2-hour fasting for clear fluids prior to surgery (26). However, there is emerging evidence over the safety of unrestricted clear fluids right up until the time of surgery and the benefits of reducing post-operative nausea rates (27).

### *Venous thromboembolism prophylaxis*

Cystectomy patients have a 5% incidence of deep vein thrombosis after surgery (28), so the use of prophylactic low molecular weight or unfractionated heparin is recommended, alongside the use of compressive stockings and intermittent pneumatic compression devices in order to reduce the risk (16).

The incidence of symptomatic deep vein thrombosis is further reduced in the post-operative period when thromboprophylaxis is continued for up to 4 weeks from oncological pelvic surgery (29).

### *Anaesthetic pre-medication*

ERAS principles do not recommend the use of benzodiazepines prior to surgery, particularly long acting

**Table 1** Enhanced recovery protocol measures utilised in the Royal Surrey County Hospital

| |
|---|
| Preoperative measures |
| Days to weeks prior to surgery |
| • Shared decision making and surgical consent |
| • Stoma nurse review and advice |
| • Dietician review and advice |
| • Physiotherapist prehabilitation advice |
| • Patient "mentors" through local bladder cancer patient forum |
| • Cardiopulmonary exercise testing |
| • Medical optimisation |
| • Cessation of smoking |
| Day prior to surgery |
| • Admission to hospital evening prior to facilitate administration of carbohydrate pre-load, stoma site marking and phosphate enemas |
| • Starved of solid food 6 hours prior to surgery, and clear fluids stopped 2 hours prior |
| • Avoidance of mechanical bowel preparation |
| Intraoperative measures |
| Anaesthesia |
| • Standardised anaesthetic protocol |
| • Intrathecal analgesia |
| • Avoidance of long acting pre-medication |
| • Antisialagogue to reduce secretions |
| • Antimicrobial prophylaxis |
| • Intraoperative normothermia |
| • Avoid excess intravenous fluids whilst steep Trendelenburg and clamped ureters |
| • Close monitoring of potassium levels |
| • Ventilator strategy to minimise airway pressures |
| • Endotracheal tube tape to avoid venous congestion |
| • BIS monitoring to avoid excessive anaesthesia |
| • Avoidance of nasogastric tubes |
| • Aid lung recruitment and reduce cerebral oedema with sitting patient and slow wake up postoperatively |
| Surgical |
| • Robot assisted |
| • Valve less insufflation system to stabilise pneumoperitoneum |
| • Small incisions |

**Table 1** *(continued)*

**Table 1** *(continued)*

| |
|---|
| Postoperative measures |
| Anaesthesia |
| • Individualised fluid therapy with goal directed fluid therapy |
| • Early disconnection of intravenous fluids after stroke volume optimisation |
| • Encouraging oral fluids and normal diet |
| • Nutritional support |
| • Thromboprophylaxis |
| Surgical |
| • Regular oral analgesics |
| • Regular physiotherapy including deep breathing and incentive spirometry |
| • Chewing gum to reduce post-operative ileus |
| • Early removal of pelvic drain |
| • Early teaching of stoma care |

ones, as it can lead to reduced eating, drinking and movement, especially in the elderly population (8,16). If necessary, short acting benzodiazepines can aid patient anxiety and patient positioning.

### *Alvimopan*

Ileus can be a major problem after RC. Rates of up to 30% have been reported (30). A major risk factor for ileus is opioid usage. Alvimopan is a μ-opioid receptor antagonist and is not available in the National Health Service (NHS) in the United Kingdom; however, Lee *et al.* demonstrated that the use of Alvimopan led to a reduced LOS and decreased time to first bowel function from 6.8 to 5.5 days after RC (31).

## Intra-operative considerations

### *Regional anaesthesia (see also postoperative analgesia)*

Neuraxial anaesthesia is a core component of colorectal ERAS protocols, as they have been shown to provide superior analgesia whilst reducing post-operative ileus, dampening the stress response and reducing cardiopulmonary complications (16,32), and their use is strongly recommended for 48–72 hours both in colorectal and urologic surgery (8,16).

The optimum vertebral level in the use of epidural analgesia is not clear, however. Between thoracic vertebrae 9–11 have been used in RC (33,34), as has a lower position of T11–L2 whilst still identifying benefit over patient-controlled analgesia (35). No prospective studies have compared epidural insertion levels.

It is not clear whether in minimally invasive surgery epidural anaesthesia is required. Two RCTs looking prospectively at ORC *vs.* RARC identified that in RARC specifically epidural analgesia can be omitted and replaced with intrathecal analgesia (16,36). This may aid earlier mobilisation in the 48–72 hours after surgery, facilitating recovery and reduced LOS.

### *Surgical approach*

Robotic-assisted radical cystectomy (RARC) is an increasingly utilised over ORC to improve patient outcomes. Minimally invasive surgery is associated with a reduced inflammatory response, reduced risk of postoperative ileus, complications and LOS. Despite these benefits, 2013 ERAS guidelines (8) do not recommend RARC due to the lack of evidence for long-term oncological outcomes. The International Robotic Cystectomy Consortium (IRCC) has since published multi-centre oncological data identifying equivalent oncological outcomes between patients who received either RARC or ORC (37), and a USA based multi-centre RCT entitled RAZOR (38) concluded non-inferiority between ORC and RARC, having explored data from 350 patients.

Beyond oncological outcomes RARC has demonstrated possible benefit over ORC with regards to estimated blood

loss (EBL), transfusion requirements, LOS and analgesia requirements whilst an inpatient (36,39). However, this is at a cost of increased operating time—329 min in ORC *vs.* 456 min in RARC in one RCT (36).

One three arm RCT has compared the use of RARC, ORC and laparoscopic radical cystectomy (LRC) identifying that LRC and ORC had comparable operative time, but with LRC least 30-day complication rate of all 3 surgical methods. This is a possible indicator that LRC may provide the benefits of minimally invasive surgery, without the added surgical time. However, the evidence for LRC is lacking, and further data is required.

### *Anaesthetic approach*

Prospective single-intervention evidence for anaesthetic practice is major urologic surgery is lacking. Principles used in fast track surgery to facilitate recovery and reduce complications include prevention of hypoxia and hypothermia, controlled hypotension (>80 mmHg), use of short acting anaesthetic agents (e.g., remifentanil) and minimising opioid use including the use of epidural analgesia, as stated previously. Blood loss requires prompt substitution, alongside antifibrinolytic use, to maintain normovolaemia and thus oxygen perfusion (16,29).

When RARC is the surgical method of choice, specific complications include subcutaneous emphysema, pressure sores and compartment syndromes, whilst challenges such as steep Tredelenberg, prolonged pneumoperitoneum and limited access to the patient should be considered by the anaesthetist (40). As such, appropriate ventilation strategies to minimise barotrauma should be employed.

### *Peritoneal drainage*

Peritoneal cavity suction drains to identify anastomotic leaks have not been found to be beneficial in colorectal surgery (16). The application of colorectal surgical practice may not apply with regards to drains, however, as the risk of urinary leakage is higher. The EAU consensus view is that drains can be avoided in select patients, however guidance is to place a 21-CH passive drain through a port-site and removed on day 1 after surgery if there is no evidence of urinary leak (16).

### *Antimicrobial prophylaxis, including skin preparation*

Surgical site infections have been reduced in colorectal surgery by appropriate perioperative intravenous antibiotics and chlorhexidine-alcohol skin preparation (41).

The EAU along with the American Urological Association recommend a single-dose 2nd or 3rd generation cephalosporin given within 60 min of skin incision and avoiding further unnecessary antibiotic administration (41).

### *Fluid management*

Fluid management for RC can be complicated by the inability to measure production intra-operatively. Goal directly fluid therapy (GDFT) using oesophageal doppler is recommended in rectal surgery (16), and has been demonstrated to reduce postoperative ileus and nausea and vomiting in RC (42).

Restricted and balanced fluid management have been advocated (43), however, concerns lie either way due to splanchnic hypo- or hyperperfusion, leading to protracted post-operative ileus, increased complication rate and increased LOS (44). Surgeons may request restrictive fluid management in order to facilitate surgical view and anastomosis healing, evidenced by one RCT deferring hydration using norepinephrine to maintain perfusion leading to reduced complication rates and decreased LOS, including improved 1-year daytime continence and erectile dysfunction rates (45-47).

Trials in fluid management deal with ASA I and II patients, whereas patient populations in RC and major urologic surgery are often more high risk, where data is lacking. Individualised GDFT led by experienced anaesthetists is advised to ensure adequate tissue perfusion (8).

### *Temperature*

Maintenance of normothermia prevents wound infections, cardiac events, bleeding, pain and oxygen consumption in colorectal surgery (14). The EAU recommend the use of warming devices to maintain body temperature (16).

## Post-operative considerations

### *Nasogastric intubation*

Cochrane meta-analysis identified no benefit in the use of a prophylactic nasogastric tube (NGT) after major abdominal surgery, indeed more postoperative complications occurred (48). In RC early removal of NGT after first flatus revealed no increase in morbidity, LOS of

recovery of bowel transit (49). Therefore, prolonged NGT is not recommended.

### *Urinary drainage*

In abdominal and thoracic surgery early removal of transurethral urinary catheter reduces urinary tract infection rates (16,50), however, there is no study evaluating optimal timing for urethral stents following RC, or transurethral catheter following RC and orthotopic neobladder formation.

The EAU reached no consensus regarding optimal timing for catheter removal for orthotopic neobladder patients, or for removal of stents following ileal conduit formation. Further data in this area is required.

### *Postoperative ileus prevention*

Postoperative ileus related to surgical and anaesthetic approach are described previously, along with the use of alvimopan, which has been demonstrated to reduce time to first bowel motion. Beyond this, oral laxatives have been associated with decreased time to first bowel movement (8,16,51) but not in the context of ERAS. Chewing gum has also demonstrated earlier first defecation, but with no effect on LOS or comorbidity (52).

### *Postoperative nausea and vomiting (PONV)*

Multimodal anti-emetic prophylaxis should be considered for patients with a high risk of PONV, alongside anaesthetic planning to minimising PONV risk by avoiding inhalational anaesthetics, nitrous oxide and opioids (8,16). PONV can also be affected through fluid management as discussed previously. Ureteroileal stenting has been demonstrated to reduce PONV incidence in one RCT (53).

### *Postoperative analgesia*

Appropriate analgesia planning facilitates postoperative mobilisation, possibly lowering VTE and chest infection risk, alongside improving muscle strength, reducing postoperative ileus and defending against insulin resistance (4,16).

Multimodal analgesia facilitates reduced opiate use, improving bowel recovery (14). As discussed previously, epidural analgesia should be considered for superior pain relief as well as the additional stress-relieving benefits in open procedures. Paracetamol and NSAIDs are recommended in all cases unless specifically contraindicated.

In open radical cystectomy (ORC) epidural analgesia (54), patient-controlled analgesia (PCA) (55) and rectus sheath catheters (RSC) (9,56) have all been used. No prospective study compares the different methodology of providing analgesia within major urologic surgery, however, ERAS guidance strongly recommends the use of epidural anaesthesia (8). Since the publication of the ERAS guidelines, Tudor *et al.* (57) have demonstrated equal analgesia between RSC and epidural analgesia in a prospective observational study in colorectal patients, however, these patients had more frequent PCA requirements, due to lack of visceral pain not covered by RSC. Following a Cochrane review it is clear open abdominal surgery epidural analgesia is superior to PCA alone (58). Current evidence suggests regional analgesia, whether central or peripheral, is necessary for open procedures (9,16,37,54,55). Further evidence in an ERAS setting comparing epidural and rectus sheath analgesia in colorectal patients in an RCT is awaited (59).

For minimally invasive surgical techniques locoregional blocks (transabdominal plane blocks), intrathecal analgesia and intravenous lidocaine are alternatives to epidural analgesia that may be beneficial (8,16).

There is no specific prospective evidence comparing analgesia for RC in the context of ERAS (8,16).

### *Early mobilisation*

Early mobilisation is endorsed by the EAU, despite little evidence to prove its specific effectiveness (16). Nevertheless, protracted bed rest is implicated in increased VTE risk, and established ERAS protocols include the use of early mobilisation (8,14,16).

### *PO intake*

Early oral or enteral feeding is a recommended ERAS principle, and within colorectal surgery has demonstrated no difference in morbidity, anastomotic leak or dehiscence rate (16). In RC, no prospective evidence has looked at associations between early feeding and morbidity or LOS. However, normal food intake is essential to maintain body homestasis (8).

## Discussion

Reassessing the perioperative approach to major urologic surgery with the evidence demonstrated in ERAS guidelines

has led to reduced patient morbidity, unchanged mortality, and decreased LOS and complications rates, especially in RC (9-12). Evidence for procedures beyond RC is clearly needed, but the application of existing ERAS principles may serve to reduce harmful interventions previously thought to be beneficial, such as prophylactic NGT usage, prolonged bed rest or nil by mouth status, whilst evidence of effect to patient mortality and morbidity is measured. Updating the evidence for some of the individual elements is also required, in particular for analgesia. We need trials comparing different modalities within an ERAS setting for both open and laparoscopic surgery.

It is clear that since then ERAS guidelines written in 2013 for urologic surgery there have been significant advances in demonstrating RARC as a viable alternative to ORC (37-40). This meets a core aim of ERAS principles, however, the financial cost of purchasing required equipment may be a barrier to adoption. Centralisation of services may facilitate this, alongside aiding the development of pathway adoption across a multidisciplinary workforce, leading to increasingly consistent high-quality care including further analysis across specific aspects of ERAS domains.

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