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Preoperative Assessment and Perioperative Optimization of Patients Undergoing Radical Cystectomy

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to list emerging areas of perioperative optimization for patients undergoing radical cystectomy and identify critical components of an ERAS (enhanced recovery after surgery) cystectomy pathway, specifically those associated with reduced risk of gastrointestinal complications.

This AUA Update aligns with the American Board of Urology Module on Oncology, Urinary Diversion, and Adrenal. Additional information on this topic can be found in the AUA Core Curriculum section on Oncology-Bladder.

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KEY WORDS: bladder cancer, radical cystectomy, perioperative optimization

INTRODUCTION

Radical cystectomy remains the standard of care for patients with muscle-invasive bladder cancer and for some with nonmuscle-invasive disease. Despite major advances in perioperative care–including implementation of enhanced recovery after surgery (ERAS) protocols and utilization of minimally invasive surgical techniques–the morbidity and mortality of cystectomy remain significant. **Following cystectomy, perioperative mortality rates are 1%-3%, nearly two-thirds of patients experience perioperative complications, and almost one-third are readmitted within 90 days.**[1] In this Update, we discuss the optimization and management of cystectomy patients to reduce patient morbidity in the perioperative period.

THE USE OF PREHABILITATION

The incidence of bladder cancer is highest among patients in their 70s and 80s. Many also have considerable comorbid disease. This is notable as functional and comorbid status have been linked to increased hospital length of stay (LOS), risk of complications, and mortality in the postoperative period. Optimizing this at-risk population prior to cystectomy is advantageous. **Prehabilitation is the process of improving patients' functional capacity before an intervention.** This is accomplished via prescribed exercise interventions to build strength and cardiovascular capacity to improve patient resilience and enhance their participation in recovery. Importantly, many prehabilitation programs also include nutritional education and optimization.

Patient participation in prehabilitation programs. Within urology, multiple studies have demonstrated the feasibility of prehabilitation programs.[2] These programs ranged from 2- to 6-week interventions and combined aerobic activity with strength training. Initiatives include a mixture of supervised exercise sessions completed in a health care facility,[2] as well as unsupervised exercises to be completed at home. Unsupervised home exercises may be well suited for low-resource patients or those without time to participate in monitored exercise programs. Examples of home exercise programs include a 4-week program, performed 3 times per week, consisting of 40 minutes of aerobic activity (walking, jogging, cycling) and 25 minutes of muscle-strengthening activity performed with elastic resistance bands.[3] Ultimately, most patients adhered to prehabilitation exercise programs, with at least 60% engaging in the majority of monitored sessions[2,4] and 83% engaging in at-home exercise programs.[3] Participation was not impacted by baseline age or comorbidity index. Additionally, no adverse events were noted, indicating the safety of these interventions.[2]

Prehabilitation has been demonstrated to be feasible and safe; it is our belief that all patients should be screened for participation in prehabilitation programs. Certain individuals may be deemed ineligible, such as those with contraindications to exercise training (eg, skeletal metastases, symptomatic coronary artery disease). Others may choose not to participate due to the additional time and costs associated with additional appointments, travel, accommodation, caregivers, and time off from work.

Impact on physical factors and quality of life. **Prehabilitation programs significantly enhanced multiple physical domains in the postoperative period.** Distance walked[2,4] and muscle power in the lower extremities were improved. Muscle power is recognized as a surrogate for capacity to perform physical activities like climbing stairs and walking. This translated into an earlier ability to perform activities of daily living (ADLs).[4] Thus, improved physical capacity can encourage early recovery.

Participation in prehabilitation programs also improved patient-reported quality of life (QOL).[2] In qualitative interviews with prehabilitation participants, patients noted satisfaction in proactively utilizing the time before surgery to prepare for cystectomy. Additionally, their participation allowed for the development of a peer group to share common experiences and encourage one another.

Impact on surgical outcomes. **Despite promising early results, prehabilitation programs have limited impact on overall surgical outcomes, rates and severity of postoperative complications, and hospital LOS.**[5] Future studies on prehabilitation should focus on understanding the length and intensity of interventions required to impact physical domains and surgical outcomes in a randomized fashion. This research should involve multidisciplinary teams, including physical therapists, to develop regimens that take a multimodal approach. **However, in the absence of adverse events associated with prehabilitation programs, it remains appropriate for patients to participate in structured physical activity while awaiting cystectomy.**

PREOPERATIVE NUTRITIONAL OPTIMIZATION

Complications related to cystectomy include malnutrition, sarcopenia (loss of skeletal muscle mass and strength), bone loss or fractures, and ileus or gastrointestinal complications.[6] **Nearly one-third of patients are malnourished before undergoing cystectomy, putting them at greater risk for postoperative complications and mortality.**[6] Furthermore, the sarcopenia that occurs with aging and oncologic disease can cause further muscle deterioration. This may be further accelerated by neoadjuvant chemotherapy and the catabolic nature of cystectomy, with as many as 81% of patients presenting with sarcopenia following these therapies. **Ultimately, patients with sarcopenia undergoing cystectomy have lower overall survival and higher cancer-specific mortality.**[7] Therefore, identifying patients who are sarcopenic and intervening to promote muscle anabolism and combat malnutrition are crucial. Conventional measures of sarcopenia rely on subjective "eyeball tests" but do not adequately describe risk. Conversely, CT cross-sectional images of the psoas, paraspinous, and thigh muscles offer reliable measures of sarcopenia.[8]

ABBREVIATIONS: activities of daily living (ADLs), enhanced recovery after surgery (ERAS), length of stay (LOS), nothing by mouth (NPO), quality of life (QOL), venous thromboembolic (VTE)

AUA Guidelines recommend that all patients undergoing cystectomy receive nutrition counseling in preparation for surgery to optimize their nutritional status. Using validated tools, such as the Patient-Generated Subjective Global Assessment, to screen for and assess the degree of malnutrition is key in triaging patients. Dietitians can assess patients' ability to eat and guide them to consume adequate protein, nutrients, and calories to prepare for surgery. Data on immunonutrition, which is the modulation of the immune system through nutrients, for patients undergoing cystectomy are still preliminary. Currently, immunonutrition before and after cystectomy is being tested in a phase 3 clinical trial to determine if this regimen reduces the risk of postoperative complications and infections (ClinicalTrials.gov identifier: NCT03801954). Screening, assessing, and then monitoring patients throughout the perioperative period are key to promote healing, preserve muscle mass and function, manage gastrointestinal issues, and assess and correct nutrient imbalances to promote long-term health.[6,9] Ideally, using muscle-supportive nutrients–such as high-quality protein, sufficient vitamin D, and β-hydroxy-β-methylbutyrate–and resistance exercise in this patient population was the best approach for minimizing muscle loss and achieving optimal restoration of functional capacity and health.[9]

ERAS protocols also recommend carbohydrate loading prior to surgery. Carbohydrate loading involves the consumption of clear carbohydrate drinks the night prior to surgery (100 g) and up to 2 hours before surgery (50 g). This reduces postoperative insulin resistance, reduces nitrogen and protein losses, preserves skeletal muscle mass, and reduces preoperative thirst and hunger. Carbohydrate loading has also been associated with a reduced LOS in major abdominal surgery (mean difference, −1.66 days; 95% CI, −2.97 to −0.34).[10] Despite the demonstrated benefits of carbohydrate loading, this process has not been adopted by many centers due to the common practice of "NPO [nothing by mouth] after midnight" to avoid pulmonary complications. However, recent literature has not found an association between aspiration and a shortened fluid fast. The American Society of Anesthesiologists, Royal College of Anaesthetists, American Society for Enhanced Recovery, and the Perioperative Quality Initiative all recommend the consumption of clear fluids 2 hours prior to surgery. **Urologists should work with their institutional perioperative and anesthesia teams to clarify NPO timing and promote the concept of carbohydrate loading 2 hours prior to surgery.**

PREOPERATIVE EXPECTATION SETTING

Given the significant morbidity of cystectomy, it is imperative that patient expectations are accurately set. Across all surgical fields, congruence of presurgical patient expectations with postsurgical outcomes has been shown to improve patient satisfaction and perioperative experience.[11] Thus, an explicit review of patients' anticipated hospital and postdischarge course, as well as their residual morbidity, is important. Since precystectomy physician encounters are often complex and limited in time, this education can be performed by staff, or via written material, support groups, and online resources. The Bladder Cancer Advocacy Network has patient-centered resources, including videos on patients' experiences with bladder cancer care and cystectomy.

Return to physical activity. Patients are often given postoperative activity restrictions, such as no lifting more than 10 lb for 6 weeks. These restrictions are based on dogma and may impede patient progress in recovery. Qualitative studies examining recovery after cystectomy found that postsurgical complaints such as fatigue, pain, and anorexia further limited patients' level of activity. Additionally, patients expressed concern that postoperative exercise may put pressure on their stoma or counteract their healing process. **Thus, it is not surprising that within the first week after cystectomy, patients are estimated to ambulate around one-third as much as their baseline.[12] Yet those who ultimately spoke to their surgeon about being physically active were more likely to do so.** Thus, specific recommendations on postoperative activity milestones may not only normalize patients' experiences, but also encourage quicker recovery to baseline levels. Ultimately, not every patient is the same. A patient's postoperative activity goals should be individualized based upon their abilities with most patients able to safely tolerate a more liberal, yet gradual, return to baseline activity levels.

Although everyone recovers at a different rate, studies show that on average it takes patients 3 months to return to their physical activity baseline. A prospective randomized controlled trial comparing open to robotic cystectomy revealed that patients were ambulating at 75% of their baseline by 5 weeks postoperatively and at baseline by 3 months.[12] This finding was reiterated by a multicenter trial that showed a significant decline in patients' ability to perform ADLs at 1 month postoperatively, yet full recovery for ADLs, independent ADLs, and the Timed Up & Go walking test by 3 months.[13] Our institutional data show that patients can perform ADLs by 1 month postoperatively with continued recovery toward their baseline through 3 months. However, we found a significant decrease in moderate-intensity exercise, such as vacuuming and mowing the lawn, at 1 month.

Sexual function. Cystectomy has significant effects on sexual function for both men and women with up to 80% of patients reporting sexual dysfunction postoperatively. In men, damage to cavernosal nerves leads to erectile dysfunction in 40%-89% of patients, even if nerve-sparing techniques are performed. In women, partial vaginectomy, devascularization of the clitoris, and damage to female neurovascular bundles can lead to anorgasmia in 45%, decreased vaginal lubrication in 41%, and dyspareunia in 22%. **Not surprisingly, patients reported lower sexual function QOL scores at 6 months after surgery. Yet, unlike many other QOL component scores, there was minimal improvement in these scores even by 24 months.[14]** Further, sexual dysfunction disproportionately affects patients under the age of 65. Explicit discussion of these side effects and available treatments should be reviewed preoperatively per AUA Guidelines.

QOL and patient satisfaction. Changes in patient-reported QOL scores mirror physical activity metrics. **Specifically, studies show that physical health–related QOL was 78% of baseline at 1 month following cystectomy and returned to baseline by 3 months.[12]** However, similar evaluation of psychological health–related QOL showed these metrics did not return to baseline until 1 year after surgery, suggesting patients continue to adjust during the first year after surgery despite returning to their physical activity baseline earlier.

A review of patient satisfaction with cystectomy found that 53%-76% of patients were satisfied with their decision to pursue surgical treatment.[15] Although these rates are relatively high, urologists should continually aim to improve patient satisfaction. Research outside of urology found that patient satisfaction after surgery was improved when tests and procedures were explained thoroughly, robust informed consent was obtained, and recovery instructions and expectations at discharge were accurately portrayed.[16]

THE USE OF ERAS PATHWAYS

ERAS pathways utilize evidence-based protocols to optimize perioperative care. **Within urology, research supports the benefits of ERAS protocols on return of bowel function, hospital LOS, and rates of complications following cystectomy. Despite this, they have not impacted rates of hospital readmissions or postoperative mortality.**[17] Important components of an ERAS cystectomy program are summarized in Table 1.

Despite considerable variability in ERAS protocols between institutions, certain protocol items are highly congruent between centers. For example, 96% of ERAS protocols omitted the use of mechanical oral bowel preparations preoperatively, 92% ensured nasogastric tubes were removed by the end of surgery, and 84% utilized medications to promote early return of bowel function, most commonly with metoclopramide (44%), alvimopan (24%), or neostigmine (8%). Further, 96% of protocols encouraged early oral feeding, with around half of these studies defining this as solid food intake before postoperative day 2.

Prior to the utilization of ERAS pathways, major contributors to prolonged hospital stays following cystectomy were paralytic ileus and other gastrointestinal complications. Early oral feeding and chewing gum are now part of the ERAS guidelines for perioperative care. It is critical for centers that endeavor to perform cystectomy to have well-designed ERAS protocols in place, with plans for goal-directed fluid management, use of medications such as alvimopan, and utilization of narcotic-sparing pain regimens to avoid gastrointestinal complications. Pharmacological agents to reduce rates of postoperative ileus are highlighted in Table 2.

Goal-directed fluid management. Excess fluid resuscitation and hypovolemia alike can cause splanchnic hypoperfusion, which may provoke bowel ischemia and ultimately the development of an ileus. Esophageal Doppler to maximize stroke volume and guide resuscitation is frequently utilized within colorectal ERAS protocols. **Within urology, a double-blinded, randomized, controlled trial compared the effect of esophageal Doppler–guided cardiovascular optimization during cystectomy to standard of care and showed a significant reduction in rates of ileus at 7% vs 18%.**[18] This study highlights the potentially deleterious effects of overresuscitation during cystectomy and the short period during which it can happen. For those without access to esophageal Doppler during cystectomy, a restrictive intraoperative fluid approach may reduce LOS, complications, and rates of postoperative ileus. Robotic and open radical cystectomy literature both support a postoperative "zero" fluid balance, resulting in zero weight gain on postoperative day 1. Fluid goals include a maximum of 3 mL/kg/h of crystalloid for robotic approaches, and 1 mL/kg/h until the bladder is removed and 3 mL/kg/h thereafter for open cystectomy.[19]

The use of alvimopan. Alvimopan is a cornerstone of current ERAS pathways and has been shown to improve return of bowel function and overall hospital LOS. In a multicenter, double-blind, placebo-controlled trial, the impact of alvimopan was compared to placebo on gastrointestinal recovery and early postoperative outcomes.[20] **Patients on alvimopan had a shorter mean time to first bowel movement by 1.3 days, which equated to a shorter mean hospital LOS by 2.6 days and no change in readmission rates.** Additionally, cost analyses show that despite higher pharmacy

Table 1. Components of a Cystectomy Program

Prehabilitation • Exercise programs include aerobic endurance training and resistance exercises • Programs vary: ◦ Total length: 2 wk-few mo ◦ Daily time: 15 min-1.5 h ◦ Frequency: once per wk- daily Nutritional optimization • Screen and assess for malnutrition • Involve dietitians who prescribe individualized food-based interventions • Use nutritional supplements, including protein Expectation setting • Discuss morbidity (effects on physical activity, sexual function, QOL) and mortality • Consider resources for improved education, including online resources	ERAS pathways • Omit oral bowel preparation • Limited use of nasogastric tubes • Allow early oral feeding and chewing gum • Employ medications to promote bowel recovery, such as alvimopan • Incorporate goal-directed fluid resuscitation • Preference nonnarcotic pain medications	Ureteral stent management • Consider use of peristent removal antibiotic prophylaxis • Check for urine leak prior to stent removal, consider JP bulb creatinine • Timing of removal variable: 5 d-3 wk Extended venous thromboembolic prophylaxis • Use low-molecular-weight heparin for 4 wk • Factor Xa oral anticoagulants may also be an option Remote monitoring • Many patients are interested in remote monitoring • Incorporation into postradical cystectomy care is feasible

Abbreviations: ERAS, enhanced recovery after surgery; JP, Jackson-Pratt; QOL, quality of life.

Table 2. Pharmacological Agents to Reduce Postoperative Ileus

Pharmacological agent	Mechanism of action	Effect
Nonsteroidal anti-inflammatory[39]	1. Reduction in opioids by 18%-51% 2. COX-derived prostaglandin effect on inflammatory response to gut handling	1. Decreased time to flatus (–9.44 h, $P = -.02$) 2. Decreased time to pass stool (–12.09 h, $P < .001$) 3. Decreased time to tolerate diet (–11.93 h, $P < .001$)
Gum chewing[40] (3 times daily from POD 0 until oral intake)	1. Feeding stimulates vagal cholinergic stimulation of gastrointestinal tract 2. Release of gastrin, pancreatic polypeptide, neurotensin which increase gastrointestinal motility 3. Reduces inhibitory sympathetic signals	1. Decreased time to flatus (2.1 vs 3.2 d, $P < .01$) 2. Decreased time to pass stool (3.1 vs 5.8 d, $P < .01$)
Alvimopan[41] (12 mg 30 min-5 h before surgery, then twice daily for up to 7 d while hospitalized, not to exceed 15 total doses)	Competitive inhibition with opiates in GI tract for μ-opioid receptors to improve gut motility	1. Lower postoperative ileus (OR 0.24, $P = .02$) 2. Decreased length of hospitalization (–0.2 to –1.6 d)
Prucalopride[42] (2 mg/d. Start 24 h after surgery. Stop after defecation, or maximum of 7 d)	Serotonin (5-HT4) receptor agonist that binds to enteric neurons. Leads to cholinergic, nonadrenergic, and noncholinergic neurotransmission that accelerates colonic transit, but not gastric or small-bowel transit	1. Decreased time to pass stool (65 vs 94.5 h, $P = .001$) 2. Decreased time to flatus (53 vs 73 h, $P < .001$) 3. Decreased length of hospitalization (7 vs 8 d, $P = .001$)
IV lidocaine[43] (1-2 mg/kg/h infused beginning at time of surgery for up to 24 h)	1. Suppresses inflammation of the obstructed gut 2. Decreases plasma extravasation and gut swelling 3. Reduction of opioid use	1. Decreased time to pass stool (–9.54 h, $P = .04$) 2. Lower postoperative ileus (OR 0.32, $P = .02$)

Abbreviations: COX, cyclooxygenase; GI, gastrointestinal; IV, intravenous; OR, odds ratio; POD, postoperative day.

charges accrued with alvimopan use, this regimen significantly decreases the overall cost of hospital care following cystectomy by decreasing the LOS.[21]

Current recommendations are to administer 12 mg alvimopan 30 minutes to 5 hours before surgery, then twice daily for up to 7 days.[22] Alvimopan is generally well tolerated. The most common adverse reaction is dyspepsia (6.1%). Patients recently exposed to opioids may have a higher incidence of gastrointestinal adverse reactions with alvimopan, and thus use is contraindicated in those taking opioids for 7+ consecutive days prior to alvimopan. Use of alvimopan is contraindicated in patients with severe hepatic impairment and end-stage renal disease. A boxed warning in the prescribing information states that alvimopan is indicated for short-term (<15 doses) hospital use only, as long-term use has been associated with increased incidence of myocardial infarction.

Postoperative pain control. ERAS protocols commonly encourage the use of nonnarcotic medications for postoperative pain control. **ERAS Society guidelines recommend use of multimodal narcotic-sparing analgesia with acetaminophen and nonsteroidal anti-inflammatory drugs.**[23] Recommendations from the ERAS Society are supported by data within colorectal surgery, and strongly encourage the use of epidural anesthesia for 72 hours following cystectomy. However, there is limited evidence within urology regarding the benefit of epidural anesthesia on pain control and return of bowel function. In a retrospective study comparing epidural anesthesia to intravenous morphine, there was no difference in return of bowel function and hospital LOS.[24] In practice the use of epidurals is limited, with only 60% of published ERAS protocols utilizing epidural anesthesia.[23] Strategies for pain control are summarized in Table 3.

URETERAL STENT MANAGEMENT

Ureteral stents are believed to better align ureteroenteric anastomoses and prevent urine leak and ureteral obstruction secondary to edema. However, inflammation from an indwelling foreign body, mucus plugging causing collecting system obstruction, and infectious complications associated with the use of stents are cited as reasons against their utilization at the time of urinary diversion.

Stent-associated morbidity. **Studies comparing the impact of ureteral stents on rates of urine leak, gastrointestinal**

Table 3. Pain Management Strategies in Enhanced Recovery After Surgery Protocols

Medication	Mechanism of action	Dosing	Data
Transdermal lidocaine	Blocks voltage-gated sodium channels, preventing propagation of nerve impulses on A delta and C fibers regulating pain 1. Suppression of local inflammation 2. Reduction of nociceptive transmission	Lidoderm patch (5% or 700 g). Apply 3 patches to painful area for 12 h on, 12 h off. Only FDA approved for neuropathic pain secondary to postherpetic neuralgia, although multiple off-label uses.	In ventral hernia repair[44]: Reduction in visual analogue pain score (3.13 vs 4.8, $P = .0067$)
Ketorolac	Competitive inhibition of COX and prostaglandin to reduce inflammation	15-60 mg IM/IV	In radical cystectomy patients[45]: A ketorolac infusion (vs morphine infusion) led to: Equal number of patients satisfied with pain management (49% vs 54%, $P = .632$) Reduced time to flatus, bowel movement, and initiation of clear liquid diet
Acetaminophen	Inhibition of COX and prostaglandin to reduce inflammation	IV, PO, rectal IV benefits: 1. Faster onset of analgesia 2. More predictable pharmacokinetics and pharmacodynamics IV downsides: 1. Infection, phlebitis, local irritation 2. Longer administration time (15 min) 3. Higher costs (approximately $40 per administration)	In postsurgical nonabdominal surgeries[46]: Mixed findings regarding improvement in pain relief between PO vs IV acetaminophen. IV formulations should only be used when PO options not available
Gabapentinoids	Not well understood 1. Reduction in opioid consumption 2. Reduction in pain may be secondary to their sedative properties	Not well defined	In radical cystectomy patients[47]: Decrease in visual analogue pain score immediately (1.6 vs 4.2) and 2 h after surgery
Epidural	Local anesthetic and/or opioid into the lumbar epidural space, which diffuses into the subarachnoid space to act on spinal nerve roots, spinal cord, and paravertebral nerves	Various dosing 1. Onset of anesthesia: 10-20 min 2. Duration of anesthesia: up to several h 3. Location: cervical, thoracic, or lumbar 4. Epidural catheter may be left in place to deliver boluses or continuous infusion up to several d	In radical cystectomy[48]: 1. Increased 30-d readmission (30% vs 26%, $P < .001$) 2. Increased median length of stay (9.0 vs 8.0 d, $P < .01$) 3. Increased rate of postoperative MI (2.6% vs 1.3%, $P < .001$)
TAP block	Local anesthetic between transversus abdominis and internal oblique muscles 1. Targets intercostal, subcostal, iliohypogastric, ilioinguinal nerves 2. Targets somatic, not visceral analgesia 3. Affects T6-L1 thoracolumbar nerves	Various	In radical cystectomy[49]: 1. Lower POD 0-3 opioid usage (106.4 vs 192.2 morphine mEq, $P = .004$) 2. Shorter length of stay (5.6 vs 7.7 d, $P < .001$)
Quadratus lumborum block	Local anesthetic anterior to quadratus lumborum and posterior to transversalis fascia 1. Targets iliohypogastric and ilioinguinal nerves 2. Affects T12-L2 thoracolumbar nerves	Various	In open radical cystectomy[50]: Quadratus lumborum block had no statistically significant difference in opioid rescue consumption compared to epidural

Abbreviations: FDA, food and drug administration; IM, intramuscular; IV, intravenous; MI, myocardial infarction; PO, oral; POD, postoperative day; TAP, transverse abdominal plane.

complications, ureteral stricture formation, and infectious complications are mixed. Data suggest that omission of ureteral stents prompted a higher rate of urine leak in the early postoperative period, as well as a significantly higher rate of nausea/vomiting and delayed return of bowel function.[25] However, there was no difference in hospital LOS between both groups. The risk of benign ureteral stricture following nonstented anastomoses ranged between 0% and 12.7%, and stented between 0.9% and 10%.[26] The average time to stricture formation was 10 to 12 months, and most patients were asymptomatic at the time of presentation.[26] These findings highlight the use of routine follow-up imaging not only to monitor for disease recurrence, but also for the development of benign strictures.

Use of peristent removal antimicrobial prophylaxis. Studies have shown that a significant number of urinary tract infections occur following ureteral stent removal.[27,28] Specifically, in a single-center retrospective study, 4.8% of patients developed bacteremia and 10.9% developed a complicated urinary tract infection within 24 hours of ureteral stent removal.[27] This accounted for one-quarter of all bacteremic episodes and one-third of all urinary tract infections within 30 days of surgery. AUA Guidelines do not specifically address antimicrobial coverage for ureteral stent removal following urinary diversion. **However, the use of antimicrobial prophylaxis significantly reduces the rate of infections following stent removal.[28]** Institutional guidelines for peristent pull antibiotics should be developed among interdisciplinary teams and adjusted to local patterns of common urinary pathogens and antimicrobial resistance.[27]

Timing of stent removal. There is variability in the timing of stent removal. Some studies recommend removal when postoperative milestones are met, while others recommend removal at postoperative time points ranging from postoperative day 5 to week 3. Within the endourology literature, animal models showed significant ureteral dilation occurs during the first 5 days after stent placement, with minimal change in ureteral diameter subsequently.[29] This change in ureteral size was matched by an increase in ureteral compliance. These data may offer physiologic support for maintaining ureteral stents until postoperative day 4 or 5. Finally, prior to stent removal, it is prudent to evaluate for urine leak via creatine assessment of pelvic drain fluid.

EXTENDED VENOUS THROMBOEMBOLISM PROPHYLAXIS

Venous thromboembolic (VTE) events are a leading cause of death among patients with cancer. Among cystectomy patients, contributing risk factors for VTE events include active malignancy, neoadjuvant chemotherapy, and recent pelvic surgery.[30] **Following cystectomy, the rate of clinically evident VTE events is estimated between 3% and 12%. Notably, more than half of these events occur after hospital discharge, on average around postoperative day 15 to 20.[30]** Considering the risk and timing of VTE events, extended VTE prophylaxis following cystectomy has been integrated into practice.

Outside of urology, a meta-analysis of prospective, randomized, controlled trials evaluating extended VTE prophylaxis after oncologic abdominal and pelvic surgeries showed a decrease in the risk of VTE events among patients receiving extended prophylaxis.[31] **These results have been reproduced within urology, with a significant decrease in the rates of VTE events following cystectomy from 12% to 5% with a 28-day regimen of enoxaparin.[32]** Although AUA Best Practice Statements do not comment on the use of extended venous thromboembolism prophylaxis following cystectomy, administration of low-molecular-weight heparin for 4 weeks postoperatively is supported by multiple surgical and oncologic panels.[30] Enoxaparin is commonly the agent of choice.

The risk of bleeding on extended VTE prophylaxis. While there is a theoretical concern for increased bleeding risk on extended VTE prophylaxis, studies show no change in the rate of postoperative transfusions.[32] This finding has been confirmed within a meta-analysis of prospective, randomized, controlled trials for oncologic abdominal and pelvic surgery, where the rate of major bleeding events was no different with the addition of extended VTE prophylaxis, at 1.8%.[31]

The use of oral anticoagulants. The use of factor Xa oral anticoagulants, such as apixaban, for extended VTE prophylaxis has gained traction. A multicenter, randomized, controlled trial including patients with gynecologic malignancies comparing 28-day courses of apixaban and enoxaparin showed no difference in the rate of VTE events, 1.0% for the apixaban group vs 1.5% for the enoxaparin group, as well as bleeding events, 0.5% for both groups.[33] However, patient satisfaction was significantly higher in the apixaban group due to the ease of medication administration and avoidance of injection-site pain. Within urology, a retrospective study on the use of apixaban following cystectomy reported no VTE events or major bleeding events within 90 days postoperatively.[34] **Thus, oral apixaban is an equivalent treatment option for extended VTE prophylaxis, with improved ease of administration and patient satisfaction.**

Blood transfusions. Radical cystectomy is associated with a frequent need for blood transfusions. Intraoperative and postoperative rates of transfusion range from 30% to 63%.[35] Transfusion may be lifesaving, but it also carries risks such as circulatory overload for patients with preexisting cardiopulmonary disease which is not uncommon in those undergoing radical cystectomy. Additional risks include incompatibility, transmission of infectious agents, coagulopathy, and allergic reactions. **Finally, the use of blood transfusions has been described as an independent negative prognostic factor for cancer recurrence, overall survival, and cancer-specific survival during radical cystectomy.[35]** Five-year cancer-specific survival is lower in those requiring intraoperative (48% vs 67%, $P < .001$) and postoperative (48% vs 63%, $P < .001$) blood transfusions.[35] This rationale has been well described.[36] Transfer of growth factors in red blood cells may promote tumor growth after transfusion, and transfusion may lead to an immunosuppressive effect which decreases tumor surveillance. As a result, many authors recommend a restrictive approach to blood transfusions during radical cystectomy, although the relationship between transfusion and overall survival on bladder cancer remains complex and controversial.[35]

USE OF REMOTE MONITORING

An increase in the use of wearable devices with health-monitoring features like pulsometers and pedometers holds the potential for augmented patient management after cystectomy via continuous,

noninvasive monitoring. Using data from these devices, providers could not only collect information on patient activity levels and vital signs, but also detect early changes in these parameters that may predict the development of postoperative complications and prompt early intervention. Patients have shown willingness to integrate remote monitoring technology into their postoperative urology care. A single-center survey revealed that 82% of patients were willing to incorporate these devices into their treatment and 20% already owned such devices.[37]

Feasibility studies following cystectomy continue to build evidence for use of these devices. For example, one study provided commercially available heart rate and fitness trackers to patients following cystectomy.[38] On average, patients wore these devices 60% of the prescribed time. Over the initial 30 days postoperatively, 5 patients experienced postoperative complications, including a readmission for infection and visits for dehydration. While there was no difference in the parameters collected between those with and without complications, this study indicated the feasibility of implementing remote monitoring in the postcystectomy population. Additional work is needed to incorporate remote monitoring into postcystectomy care and explore the potential patient benefit of this practice.

CONCLUSIONS

This Update is not an exhaustive list of considerations on the topic of optimization of radical cystectomy patients, but instead is meant to examine some of the critical components of high-quality perioperative care as well as innovations within the field. For additional information, please refer to the AUA White Papers on the topic of perioperative patient optimization.

DID YOU KNOW?

- Radical cystectomy is associated with significant associated morbidity and mortality. Emerging initiatives aimed at optimizing patient outcomes include prehabilitation, preoperative nutritional optimization, incorporation of factor Xa oral anticoagulants for extended VTE prophylaxis, and integration of remote monitoring into postoperative care.
- Explicit preoperative expectation setting is critical prior to radical cystectomy. While every patient's postoperative course is unique, studies show many can anticipate returning to their baseline activity levels by 3 months postoperatively.
- Multiple components of ERAS protocols following radical cystectomy focus on evidence-based management of risk factors associated with delayed return of bowel function. Incorporation of goal-directed fluid management, use of μ-receptor antagonists, and avoidance of narcotic pain medications have all been shown to reduce the risk of gastrointestinal complications in the postoperative period.
- Following radical cystectomy, the rate of VTE events is between 3% and 12%. These typically occur on postoperative day 15 to 20. Use of low-molecular-weight heparin for 4 weeks postoperatively has been shown to reduce the risk of VTE events. Oral apixaban has been shown to be an equivalent treatment option for extended VTE prophylaxis in randomized control trials outside of urology.

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1. Following radical cystectomy, what is the risk of perioperative mortality?
   a. <1%
   b. 1%-3%
   c. 4%-5%
   d. 6%-7%

2. The use of prehabilitation before radical cystectomy results in
   a. Improved physical fitness and improved rates of readmission
   b. No change in physical fitness, yet improved rates of readmission
   c. Improved physical fitness, yet no change in rates of readmission
   d. No change physical fitness and no change in rates of readmission

3. A 65-year-old female is scheduled to undergo radical cystectomy for muscle-invasive bladder cancer. According to ERAS protocols, what additional recommendation should be made to her regarding nutritional intake prior to cystectomy?
   a. Nothing by mouth (NPO) after midnight
   b. NPO after midnight, with carbohydrate loading via consumption of whole grains, on the night before surgery
   c. NPO after midnight, with carbohydrate loading via consumption of clear liquids, on the night before surgery
   d. Carbohydrate loading via consumption of clear liquids on the night prior to surgery, and up to 2 hours before surgery

4. The majority of venous thromboembolic (VTE) events occur during which perioperative period surrounding radical cystectomy?
   a. Intraoperatively
   b. Postoperative day 3 to 7
   c. Postoperative day 15 to 20
   d. Postoperative day 25 to 30

5. A 65-year-old female underwent uncomplicated open radical cystectomy 5 days ago. She has met all her milestones for discharge. She has no history of DVT or PE and has been receiving 40 mg daily enoxaparin intramuscularly for DVT prophylaxis while hospitalized. Upon discharge, the patient asks why you have transitioned her to oral apixaban for DVT prophylaxis. What is your reasoning?
   a. More affordable
   b. Improved ease of administration and patient satisfaction
   c. Lower rates of DVT and PE as compared to enoxaparin
   d. More stable pharmacokinetics