

Paper Alert

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Radical cystectomy is the gold standard treatment for muscle invasive (stage T2 – T4a) bladder cancer, but is associated with a high incidence of complications, readmissions, and mortality [1–3] partially because of the magnitude of surgery and partially because of the significant comorbidity burdens patients who develop this disease have [4, 5]. Aside from reduced blood loss, as opposed to renal and prostatic surgery, advantages of minimally invasive cystectomy, despite claims from retrospective clinical series, have not been borne out in randomized prospective assessments [6], although the results of larger studies are pending. However what is clear is that adopting information gained from colorectal surgery, enhanced recovery after surgery (ERAS) protocols have resulted in considerably shorter lengths of hospital stay (LOS) without increasing postoperative complications or readmissions. Two recent publications [1, 7] and two structured reviews [8, 9] confirm this. However the diffusion of many aspects of ERAS protocols has not occurred although many urologic oncologic surgeons claim to adhere to them [10]. Despite this, because of improved intensive, anesthetic and perioperative care, and increased centralization of cystectomy surgery, more cystectomies are being performed with lower operative/postoperative mortalities and improved long-term survivals [3].

Factors impacted by ERAS protocols are enumerated in two recent structured reviews [8, 9]. These highlight the need for intensive preoperative nutritional assessment, comprehensive patient education by many caregivers (i.e. surgeons, gerontologists, anesthesiologists, nurses, wound-ostomy

specialists), excellent communication between surgical and anesthesia teams, minimized preoperative dehydration/starvation, preoperative carbohydrate loading, omission of nasogastric tubes or removing them immediately after surgery, attention to intraoperative and postoperative pain management, limited use of opioid narcotics, early postoperative ambulation and feeding, routine use of intra- and postoperative venous thrombo-embolic (VTE) prophylaxis, and intensive post hospital discharge monitoring and follow-up. Moreover, accurate monitoring of intra- and postoperative adherence to protocol is critical, not only in documenting events for scholarly and quality improvement purposes, but also making certain that patients do not “slip through the cracks”. This is a fundamental shift for most urologists and most bladder cancer patients, who, because of their advanced age and comorbidities [5], as well as their variable disease states, represent a very challenging set of patients to fit into any regimented protocol. That several of the published series have reported outcomes in consecutive patients with limited or no exclusions [1] attests to the effort expended by those choosing to carry out these programs.

While modifications to these protocols have occurred, and clearly some patients cannot receive all elements – some key factors, a few of which have been supported by level 1 evidence in radical cystectomy patients, merit mentioning: 1 – the use of Alvimopan, a peripherally active μ -opioid receptor antagonist, with a single preoperative oral dose and twice/day oral doses post operatively for up to 7 days unequivocally reduces opioid induced ileus and speeds up return of postoperative bowel function [11], and 2 - some form of intraoperative fluid restriction also results in less postoperative ileus and a lower need for transfusions [8, 9, 12, 13].

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With these and other supporting data [1, 7], how often do urologists enact ERAS protocols? A survey was sent to Society of Urologic Oncology members with a self-identified special interest in bladder cancer, asking whether they consider themselves ERAS adapters and inquiring specifically about adherence to seven components of virtually all ERAS protocols (comprehensive preoperative education, bowel preparation avoidance, nasogastric tube avoidance, intraoperative normothermia, opioid avoidance, early ambulation, and early feeding) [10]. While nearly half of the bladder cancer surgeons contacted responded to the survey, and 64% of respondents considered themselves to adhere to ERAS principles for cystectomy, only 20% practiced all 7 interventions. It is not surprising that their average LOS was self-reported at 6.1 days, while for the series with stricter adherence to ERAS principles LOSs from 3–5 days were routinely reported [1, 7]. It is probable that had the survey involved the rigid monitoring and archiving used by these and other groups, rather than self-reporting, longer LOSs and even less adherence would have been found [10].

But while considerable progress in optimizing recovery from cystectomy has occurred, further improvements in care of cystectomy patients seems quite possible. Relatively ‘low hanging fruit’ include enhanced preoperative and postoperative immuno-nutrition, more standardized management of intraoperative and postoperative fluids, and rigorous postoperative stent management and removal protocols, could all reduce short term complications and readmissions.

But despite relatively limited adoption of ERAS protocols and the existence of obvious areas where improvements are needed, we are doing better.

Using the United Kingdom’s National Cancer data repository for 1998–2010 [3], Hounsoms and colleagues – reported a 56% increase in RCs performed per year (from 969 in 1998–2000 to 1496 in 2008–2010) despite a stable number of new cases of bladder cancer being diagnosed during the same interval. Deaths within 30 days and 90 days after RC decreased by 59% and 50%, respectively during this time, with the greatest improvements being seen in the elderly. One and five year overall survival for RC patients improved from 71% to 80% and 49% to 56%, respectively (each $p < 0.001$). However, stage specific RC and survival/mortality rates could not be determined because of poor adherence to reporting TNM staging, so whether this improvement is due to

improved care or shift to lower stage patients undergoing RC is not certain. During this time there has been a trend to centralization of this procedure with cystectomy centers performing 3 times the number of RCs in 2010 as they did in 1998. Given that ERAS programs were only being formally rolled out in England in 2010, further improvements, particularly in short-term outcomes, can be anticipated.

REFERENCES

- [1] Kukreja JE, Messing EM, Shah JB. Are we doing “better”? The discrepancy between perception and practice of enhanced recovery after cystectomy principles among urologic oncologists. *Urol Onc* 2016;34.
- [2] Tan WS, Lamb BW, Kelly JD. Complications of radical cystectomy and orthotopic reconstruction. *Adv Urol* 2015.
- [3] Hounsoms LS, Verne J, McGrath JS, et al. Trends in operative caseload and mortality rates after radical cystectomy for bladder cancer in England for 1998-2010. *Eur Urol* 2015;6:1056-62.
- [4] Scosyrev E, Golijanin D, Wu G, et al. The burden of bladder cancer in men and women: Analysis over the years of life lost. *BJU Int* 2012;109:57-62.
- [5] Scosyrev E, Wu G, Golijanin D, et al. Non-bladder cancer mortality in patients with urothelial cancer of the bladder. *Urol Onc* 2013;31:656-63.
- [6] Bochner BH, Dalbagni G, Sjoberg DD, et al. Open radical cystectomy and robot-assisted laparoscopic radical cystectomy: A randomized clinical trial. *Eur Urol* 2015;67:1042-50.
- [7] Matulewicz RS, Brennan J, Pruthi RS, et al. Radical cystectomy perioperative care redesign. *Urology* 2015;86:1076-86.
- [8] Azhar RA, Bochner B, Catto J, et al. Enhanced recovery after urological surgery: A contemporary systematic review of outcomes, key elements, and research needs. *Eur Urol* 2016, <http://dx.doi.org/10/1016/j.eurouro.2016.02.051>
- [9] Kukreja JE, Kiernan M, Schempp B, et al. Quality improvement in cystectomy care with enhanced recovery (QUICCER Study). *Brit J Urol Int*, in press, 2016.
- [10] Lee CT, Chang SS, Kamat AM, et al. Alvimopan accelerates gastrointestinal recovery after radical cystectomy: A multicenter randomized placebo-controlled trial. *Eur Urol* 2014;66:265-72.
- [11] Wuethrich PY, Studer UE, Thalmann GN, et al. Intraoperative continuous norepinephrine infusion combined with restrictive deferred hydration significantly reduces the need for blood transfusion in patients undergoing open radical cystectomy: Results of a prospective randomized trial. *Eur Urol* 2014;66:352-60.
- [12] Pillai P, McEleavy I, Gaughan M, et al. A double-blind randomized controlled clinical trial to assess the effect of doppler optimized intraoperative fluid management on outcome following radical cystectomy. *J Urol* 2011;186:2201-6.
- [13] Xu W, Daneshmand S, Bazargani ST, et al. Postoperative pain management after radical cystectomy: Comparing traditional versus enhanced recovery protocol pathway. *J Urol* 2015;194:1209-13.