

# Advances in surgical management of muscle invasive bladder cancer

Janet Baack Kukreja\*, Jay B. Shah

Department of Urology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

\*E-mail: janet.kukreja@gmail.com

## ABSTRACT

**Introduction:** Bladder cancer remains a disease of the elderly with relatively few advances that have improved survival over the last 20 years. Radical cystectomy (RC) has long remained the principal treatment for muscle-invasive bladder cancer (MIBC).

**Methods:** A literature search of PubMed was performed. The content was reviewed for continuity with the topic of surgical advances in MIBC. Articles and society guidelines were included in this review.

**Results:** Despite the associated morbidity, even in the elderly, RC is still a reasonable option. Modifications during RC may have a positive or negative impact on survival and quality of life. The extent of pelvic lymph node dissection is one such factor which may positively impact survival outcomes. In addition, preservation of pelvic organs, robotic surgery and the adoption of enhanced recovery after surgery principles continues to improve the postoperative recovery and quality of life in RC patients.

**Conclusion:** There are some ongoing studies in many of these areas, but overall the new advances in MIBC may improve patient quality and quantity of life. The advances in surgical treatment of MIBC are important and the focus of the review here.

## INTRODUCTION

Bladder cancer remains a disease of the elderly with relatively few advances that have improved survival over the last 20 years.<sup>[1-3]</sup> Radical cystectomy (RC) has long remained the principal treatment for muscle-invasive bladder cancer (MIBC).<sup>[4]</sup> Despite the associated morbidity, even in the elderly, RC is still a reasonable option.<sup>[5]</sup> Modifications during RC may have a positive or negative impact on survival and quality of life. The extent of pelvic lymph node dissection (ePLND) is one such factor which may positively impact survival outcomes.<sup>[6]</sup> In addition, preservation of pelvic organs, robotic surgery, and the adoption of enhanced recovery after surgery (ERAS) principles continues to improve the postoperative recovery and quality of life in RC patients.<sup>[7-9]</sup> The advances in surgical treatment of MIBC are important and the focus of the review here.

## METHODS

Literature review was completed by searching the PubMed database with the term “cystectomy or bladder cancer” in addition to one of the following terms: “lymph node dissection,” “organ sparing,” “chemotherapy,” “robotic,” “laparoscopic,” or “enhanced recovery.” Included studies were available in English language and full text from institutional subscription or PubMed. Relevant studies and guideline publications were included if they were published in the last 3 years.

## ADVANCES IN SURGERY FOR MUSCLE INVASIVE BLADDER CANCER

### *Integration of systemic chemotherapy*

Survival after RC for MIBC is dependent not only on surgical techniques but also on the thoughtful integration

### Access this article online

<b>Quick Response Code:</b>	<b>Website:</b> www.indianjurol.com
	<b>DOI:</b> 10.4103/0970-1591.203416

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

**For reprints contact:** reprints@medknow.com

**Received:** 19.08.2016, **Accepted:** 22.11.2016

**Financial support and sponsorship:** Nil.

**Conflicts of interest:** There are no conflicts of interest.

of systemic therapy. Neoadjuvant chemotherapy (NAC) before RC is supported by level I evidence and continues to be recommended by multiple guidelines.<sup>[10-12]</sup> With increasing awareness and recommendations from urology and oncology organizations, there seems to be improved utilization of NAC in the MIBC patients.<sup>[13,14]</sup> Interestingly, for many years methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) has been thought to have oncological equivalence to gemcitabine and cisplatin (GC). However, a recent meta-analysis of over 3000 patients rekindles the question of which regimen is superior.<sup>[15]</sup> Yin *et al.* reported a possible advantage to MVAC compared to GC for overall survival, however, this was not statistically significant, (hazard ratio [HR], 1.31; 95% confidence interval [CI], 0.99–1.74).<sup>[15]</sup> Even in those where NAC is omitted, there is increasing evidence to support the use of adjuvant chemotherapy.<sup>[16]</sup> As new immunotherapies arise, they may provide survival advantages when combined with RC, but only future studies will be able to provide answers.<sup>[17,18]</sup>

### Extended lymph node dissection

Pelvic lymph node dissection remains integral to RC for MIBC. It is clear that a pelvic lymph node dissection with RC provides a survival advantage compared to RC alone.<sup>[19]</sup> There are many studies which suggest a direct correlation between the increasing numbers of lymph nodes removed and improved survival.<sup>[19,20]</sup> Hence, the remaining question is: does a formal ePLND provide a survival advantage? In a recent meta-analysis reported on over 2800 patients who underwent pelvic lymph node dissection, those who had  $\geq$  pT3 disease had a significant benefit in recurrence-free survival with ePLND, HR: 0.61 (95% CI: 0.52–0.73),  $P < 0.001$ , but the same did not hold true for those with  $\leq$  pT2 disease, HR: 0.95 (95% CI 0.64–1.41),  $P = 0.81$ .<sup>[20]</sup> An additional report noted patients may have more morbidity associated, specifically greater blood loss ( $P < 0.001$ ), with ePLND, but the ePLND does result in a decrease in local recurrences.<sup>[21]</sup> In patients with micrometastatic disease, the ePLND may provide greater survival benefit (HR: 0.52; 95% CI 0.43–0.64) compared to those without any occult lymph node metastasis.<sup>[22]</sup> Ongoing studies, such as SWOG 1011 phase III trial and the German Association of Urologic Oncology trial are randomized trials to compare ePLND to standard lymph node dissection and will help provide more definitive data and possibly stratify which patients benefit the most from ePLND.<sup>[10,23]</sup>

### Organ sparing

For patients who are carefully selected, sparing of the peritoneum, prostate, vagina, and uterus can provide several advantages without compromising the oncological outcomes.<sup>[24,25]</sup> Organ-sparing cannot only provide improved sexual function; it may augment urinary function.<sup>[26]</sup> An additional technique during RC which may improve the quality of life is the readaptation of the dorsolateral

peritoneal layers after ePLND. The readaptation of these peritoneal layers has been explored as an option to reduce postoperative ileus.<sup>[27]</sup> Vatolomei *et al.* reported outcomes of a randomized study looking at 200 patients with and without readaptation.<sup>[27]</sup> They found that there was less pain and better bowel function at both 3 and 24 months postoperatively.<sup>[27]</sup> In addition to the peritoneal readaptation, different degrees of other pelvic organ preservation may also be beneficial.

For men, sexual preservation has been described in several variations. For any prostate sparing treatment, it is recommended that there be no tumor at the bladder neck, a prostatic urethral biopsy is obtained before RC, and prostate specific antigen checked.<sup>[28]</sup> In addition, a transrectal ultrasound-guided prostate biopsy should be performed.<sup>[28]</sup> The first form of male preservation is nerve sparing. As with radical prostatectomy, nerve sparing does help maintain sexual function.<sup>[10,29,30]</sup> In a highly selected group, nerve sparing and seminal vesicle sparing may help preserve functional outcomes with over 70% reporting potency within 12 months of surgery; however, long-term oncological data are not available at this time, and this should be done with caution.<sup>[30]</sup> In addition, nerve sparing reports with short follow-up report oncologic outcomes are not compromised with this technique.<sup>[10]</sup> The second variation of male organ sparing is prostate capsule sparing. Sparing the prostatic capsule is supported by some and may provide theoretical advantages, however, a recent randomized control trial comparing the prostatic capsule sparing to the traditional nerve sparing at cystectomy with neobladder creation showed no benefit at 12 months in sexual or urinary function.<sup>[31]</sup> However, full prostate sparing may provide a safe oncological result with superior urinary and sexual function, in highly selected patients.<sup>[28]</sup> The last method for male sexual organ sparing reported is the bilateral nerve sparing along with the prostatic apex.<sup>[32]</sup> This approach in younger RC patients has improved sexual function; however, oncological outcomes are yet to be determined.<sup>[32]</sup>

For women absence of trigonal and bladder floor involvement, lack of palpable posterior masses on bimanual exam and absence of enlarged lymph nodes has been associated with lack of bladder cancer extension to the pelvic organs. These factors may help stratify which women should be offered nerve, vaginal, and uterine sparing RC during preoperative counseling.<sup>[33]</sup> Specifically, uterine preservation allows for avoidance of vaginal shortening, which may improve healthcare-related quality of life (HRQoL).<sup>[34]</sup> Importantly, the avoidance of vaginal shortening has been reported to improve sexual function for women.<sup>[24]</sup> In addition, uterine preservation allows for improved urinary function in women with continent diversions.<sup>[34]</sup> Urinary function may also be improved with intentional nerve sparing in women.<sup>[35]</sup>

Although the idea of sparing pelvic organs is appealing, it should be done only in selected patients. The overall quality of evidence related to organ sparing RC is not robust. Thus, RC with sparing of pelvic organs is not routinely recommended.<sup>[10]</sup>

### **Robotic surgery**

The role of robotic cystectomy remains controversial.<sup>[36]</sup> However, robotic RC has become an acceptable alternative to open surgery by some guideline organizations, including the European Association of Urology.<sup>[10]</sup>

There appear to be no compromised outcomes in survival for robotic RC patients. Multiple studies report similar oncological outcomes at 5 years for robotic RC compared to open RC.<sup>[37-40]</sup> Oncological outcomes have been subject to heavy criticism because of selection bias.<sup>[41,42]</sup> However, multiple studies have reported advanced pathology treated with robotic RC has similar oncological outcomes to advanced pathology treated with open RC.<sup>[37-41]</sup> In addition, there is no difference in lymph node yield between the two modalities.<sup>[43]</sup>

The Memorial Sloan Kettering trial, the only randomized clinical trial to date comparing open and robotic RC, only included open urinary diversions.<sup>[44]</sup> An experienced robotic surgeon can often perform an intracorporeal urinary diversion of any type and may be able to avoid postoperative gastrointestinal side effects as well as other postoperative morbidity.<sup>[10,45-47]</sup> There are no randomized trials comparing complete robotic intracorporeal urinary diversion with open RC. Robotic RC seems to be safe for patients; no studies have been published demonstrating an increase in perioperative complications.<sup>[48]</sup> Importantly, there are many reports of robotic RC having less blood loss than open RC.<sup>[36,49]</sup>

With some benefits and no oncologic compromise, the ideal patient population for robotic RC is yet to be determined. Winter *et al.* recently published a study where elderly patients specifically may be offered a benefit by robotic surgery.<sup>[49]</sup> To date, few have looked at patient-reported HRQoL outcomes. Improved physical wellbeing may be found in robotic RC when compared to open RC patients.<sup>[50]</sup> The randomized multicenter open versus robotic cystectomy (RAZOR) trial outcomes are anxiously awaited to see what advantages or disadvantages are seen with robotic RC.<sup>[51]</sup> In the meantime, robotic RC is considered effective and safe with comparable oncological outcomes.<sup>[52]</sup>

### **Enhanced recovery after surgery**

ERAS pathways for cystectomy have become gradually more popular to aid in the recovery of patients after surgery.<sup>[9,53]</sup> ERAS pathways have been long used in colorectal surgery. This has become the foundation on which enhanced recovery for RC patients was built. There are many components to these pathways to help alleviate

the physical and psychological stress RC brings to these patients.<sup>[7,9]</sup> A recent meta-analysis reported a reduction in complications and length of stay in the hospital.<sup>[8]</sup> Important components of ERAS for RC patients include: patient education, prehabilitation, carbohydrate loading, maintenance of euvolemia, maintenance of normothermia, early enteral feeding, early mobilization, opioid avoidance, multimodal pain control, and venous thromboembolism prevention.<sup>[7,9,54,55]</sup>

Part of ERAS is a focus on euvolemia. Euvolemia can be maintained by the use of hemodynamic monitoring and norepinephrine to prevent postoperative fluid overload.<sup>[56]</sup> Further, norepinephrine has been associated with decreased intraoperative blood loss and a faster return of bowel function.<sup>[56,57]</sup> One study reported improved urinary and sexual function outcomes with norepinephrine use and fluid restriction.<sup>[58]</sup>

Despite the practice of ERAS becoming more popular, there still exists a gap between the perception of practicing ERAS principles and clinical practice.<sup>[59]</sup> Only improved awareness will help urologists advance ERAS implementation which will lead to increased patient benefit.<sup>[9,59]</sup>

## **FUTURE DIRECTIONS**

The future of MIBC surgery will continue to be shaped by a multidisciplinary team. Integration of systemic immunotherapy for MIBC and RC will likely be important, especially in platinum ineligible patients. Furthermore, markers to predict patient recovery after RC and measures of RC patients' symptoms burden will give us insight into how to better counsel and prepare patients for RC. As robotic surgeons gain urinary diversion experience, this may allow streamlining of the operation and lead to an overall decrease in complications. Finally, RC currently is reserved for those who can be cured of their MIBC; the question remains as to whether there may be a life prolonging advantage in cytoreductive RC.

## **CONCLUSION**

Overall, there are some advances in MIBC surgery which can prolong survival and improve the quality of life after RC. There are still many unanswered questions in the area of surgery for MIBC, but hopefully ongoing research will provide us with more data in the near future.

## **REFERENCES**

1. Skinner EC. Treatment of muscle-invasive bladder cancer in older patients. *Am Soc Clin Oncol Educ Book* 2016;35:e228-33.
2. Grubmueller B, Seitz C, Shariat SF. The treatment of muscle-invasive bladder cancer in geriatric patients. *Curr Opin Urol* 2016;26:160-4.
3. Rose TL, Milowsky MI. Management of muscle-invasive bladder cancer in the elderly. *Curr Opin Urol* 2015;25:459-67.

4. Salama A, Abdelmaksoud AM, Shawki A, Abdelbary A, Aboukassam H. Outcome of muscle-invasive urothelial bladder cancer after radical cystectomy. *Clin Genitourin Cancer* 2016;14:e43-7.
5. VanderWalde NA, Chi MT, Hurria A, Galsky MD, Nielsen ME. Treatment of muscle invasive bladder cancer in the elderly: Navigating the trade-offs of risk and benefit. *World J Urol* 2016;34:3-11.
6. Chou R, Selph SS, Buckley DI, Gustafson KS, Griffin JC, Grusing SE, *et al.* Treatment of muscle-invasive bladder cancer: A systematic review. *Cancer* 2016;122:842-51.
7. Baack Kukreja JE, Kiernan M, Schempp B, Siebert A, Hontar A, Dolan J, *et al.* Quality improvement in cystectomy care with enhanced recovery (QUICCER Study). *BJU Int* 2016. doi:10.1111/bju.13521.
8. Tyson MD, Chang SS. Enhanced recovery pathways versus standard care after cystectomy: A meta-analysis of the effect on perioperative outcomes. *Eur Urol* 2016. pii: S0302-283830200-7.
9. Danna BJ, Wood EL, Baack Kukreja JE, Shah JB. The future of enhanced recovery for radical cystectomy: Current evidence, barriers to adoption, and the next steps. *Urology* 2016;96:62-8.
10. Alfred Witjes J, Lebre T, Compérat EM, Cowan NC, De Santis M, Bruins HM, *et al.* Updated 2016 EAU guidelines on muscle-invasive and metastatic bladder cancer. *Eur Urol* 2016. pii: S0302-283830290-1.
11. Zargar H, Espiritu PN, Fairey AS, Mertens LS, Dinney CP, Mir MC, *et al.* Multicenter assessment of neoadjuvant chemotherapy for muscle-invasive bladder cancer. *Eur Urol* 2015;67:241-9.
12. Milowsky MI, Rumble RB, Booth CM, Gilligan T, Eapen LJ, Hauke RJ, *et al.* Guideline on muscle-invasive and metastatic bladder cancer (European Association of Urology Guideline): American Society of clinical oncology clinical practice guideline endorsement. *J Clin Oncol* 2016;34:1945-52.
13. Krabbe LM, Westerman ME, Margulis V, Raj GV, Sagalowsky AI, Courtney K, *et al.* Changing trends in utilization of neoadjuvant chemotherapy in muscle-invasive bladder cancer. *Can J Urol* 2015;22:7865-75.
14. Booth CM. Perioperative chemotherapy for muscle-invasive bladder cancer: Closing the gap between evidence and practice. *Can Urol Assoc J* 2016;10:31-2.
15. Yin M, Joshi M, Meijer RP, Glantz M, Holder S, Harvey HA, *et al.* Neoadjuvant chemotherapy for muscle-invasive bladder cancer: A systematic review and two-step meta-analysis. *Oncologist* 2016;21:708-15.
16. Reardon ZD, Patel SG, Zaid HB, Stimson CJ, Resnick MJ, Keegan KA, *et al.* Trends in the use of perioperative chemotherapy for localized and locally advanced muscle-invasive bladder cancer: A sign of changing tides. *Eur Urol* 2015;67:165-70.
17. Trenta P, Calabrò F, Cerbone L, Sternberg CN. Chemotherapy for muscle-invasive bladder cancer. *Curr Treat Options Oncol* 2016;17:6.
18. Knollman H, Godwin JL, Jain R, Wong YN, Plimack ER, Geynisman DM. Muscle-invasive urothelial bladder cancer: An update on systemic therapy. *Ther Adv Urol* 2015;7:312-30.
19. Larcher A, Sun M, Schiffmann J, Tian Z, Shariat SF, McCormack M, *et al.* Differential effect on survival of pelvic lymph node dissection at radical cystectomy for muscle invasive bladder cancer. *Eur J Surg Oncol* 2015;41:353-60.
20. Bi L, Huang H, Fan X, Li K, Xu K, Jiang C, *et al.* Extended vs. non-extended pelvic lymph node dissection and their influence on recurrence-free survival in patients undergoing radical cystectomy for bladder cancer: A systematic review and meta-analysis of comparative studies. *BJU Int* 2014;113:E39-48.
21. Abdi H, Pourmalek F, Gleave ME, So AI, Black PC. Balancing risk and benefit of extended pelvic lymph node dissection in patients undergoing radical cystectomy. *World J Urol* 2016;34:41-8.
22. Wright JL, Lin DW, Porter MP. The association between extent of lymphadenectomy and survival among patients with lymph node metastases undergoing radical cystectomy. *Cancer* 2008;112:2401-8.
23. Huguenin CM, Daneshmand S. Lymph node dissection in bladder cancer: Where do we stand? *World J Urol* 2015;1-7. doi: 10.1007/s00345-015-1751-9.
24. Ali-El-Dein B, Mosbah A, Osman Y, El-Tabey N, Abdel-Latif M, Eraky I, *et al.* Preservation of the internal genital organs during radical cystectomy in selected women with bladder cancer: A report on 15 cases with long term follow-up. *Eur J Surg Oncol* 2013;39:358-64.
25. Roth B, Thalmann GN. Standard cystectomy fits all: Truth or myth? *Transl Androl Urol* 2015;4:254-60.
26. Modh RA, Mulhall JP, Gilbert SM. Sexual dysfunction after cystectomy and urinary diversion. *Nat Rev Urol* 2014;11:445-53.
27. Vartolomei MD, Kiss B, Vidal A, Burkhard F, Thalmann GN, Roth B. Long-term results of a prospective randomized trial assessing the impact of re-adaptation of the dorsolateral peritoneal layer after extended pelvic lymph node dissection and cystectomy. *BJU Int* 2016;117:618-28.
28. Mertens LS, Meijer RP, de Vries RR, Nieuwenhuijzen JA, van der Poel HG, Bex A, *et al.* Prostate sparing cystectomy for bladder cancer: 20-year single center experience. *J Urol* 2014;191:1250-5.
29. Haberman K, Wittig K, Yuh B, Ruel N, Lau C, Wilson TG, *et al.* The effect of nerve-sparing robot-assisted radical cystoprostatectomy on erectile function in a preoperatively potent population. *J Endourol* 2014;28:1352-6.
30. Asimakopoulos AD, Campagna A, Gakis G, Corona Montes VE, Piechaud T, Hoepffner JL, *et al.* Nerve sparing, robot-assisted radical cystectomy with intracorporeal bladder substitution in the male. *J Urol* 2016;196:1549-57.
31. Jacobs BL, Daignault S, Lee CT, Hafez KS, Montgomery JS, Montie JE, *et al.* Prostate capsule sparing versus nerve sparing radical cystectomy for bladder cancer: Results of a randomized, controlled trial. *J Urol* 2015;193:64-70.
32. Nyame YA, Zargar H, Ramirez D, Ganesan V, Babbar P, Villers A, *et al.* Robotic-assisted laparoscopic bilateral nerve sparing and apex preserving cystoprostatectomy in young men with bladder cancer. *Urology* 2016;94:259-64.
33. Gregg JR, Emeruwa C, Wong J, Barocas DA, Chang SS, Clark PE, *et al.* Oncologic outcomes after anterior exenteration for muscle invasive bladder cancer in women. *J Urol* 2016;196:1030-5.
34. James AC, Lin DW, Wright JL. Neobladders and continent catheterizable stomas for the bladder cancer survivor. *Curr Opin Urol* 2014;24:407-14.
35. Gross T, Meierhans R, Ruf SD, Meissner C, Ochsner K, Studer UE. Orthotopic ileal bladder substitution in women: Factors influencing urinary incontinence and hypercontinence. *Eur Urol* 2015;68:664-71.
36. Luchey AM, Agarwal G, Poch MA. Robotic-assisted radical cystectomy. *Cancer Control* 2015;22:301-6.
37. Raza SJ, Wilson T, Peabody JO, Wiklund P, Scherr DS, Al-Daghmin A, *et al.* Long-term oncologic outcomes following robot-assisted radical cystectomy: Results from the International Robotic Cystectomy Consortium. *Eur Urol* 2015;68:721-8.
38. Snow-Lisy DC, Campbell SC, Gill IS, Hernandez AV, Fergany A, Kaouk J, *et al.* Robotic and laparoscopic radical cystectomy for bladder cancer: Long-term oncologic outcomes. *Eur Urol* 2014;65:193-200.
39. Gandaglia G, De Groot R, Geurts N, D'Hondt F, Montorsi F, Novara G, *et al.* Oncologic outcomes of robot-assisted radical cystectomy: Results of a high-volume robotic center. *J Endourol* 2016;30:75-82.
40. Ahdoot M, Almario L, Araya H, Busch J, Conti S, Gonzalgo ML. Oncologic outcomes between open and robotic-assisted radical cystectomy: A propensity score matched analysis. *World J Urol* 2014;32:1441-6.
41. Raza SJ, Field E, Kibel AS, Mottrie A, Weizer AZ, Wagner A, *et al.* International Robotic Radical Cystectomy Consortium: A way forward. *Indian J Urol* 2014;30:314-7.
42. Navai N, Dinney CP. Oncologic equivalence between laparoscopic/robotic and open radical cystectomy. *J Urol* 2016;195:1646-7.
43. Davis JW, Gaston K, Anderson R, Dinney CP, Grossman HB, Munsell MF, *et al.* Robot assisted extended pelvic lymphadenectomy at radical cystectomy: Lymph node yield compared with second look open dissection. *J Urol* 2011;185:79-83.

44. Bochner BH, Sjoberg DD, Laudone VP; Memorial Sloan Kettering Cancer Center Bladder Cancer Surgical Trials Group. A randomized trial of robot-assisted laparoscopic radical cystectomy. *N Engl J Med* 2014;371:389-90.
45. Adding C, Collins JW, Laurin O, Hosseini A, Wiklund NP. Enhanced recovery protocols (ERP) in robotic cystectomy surgery. Review of current status and trends. *Curr Urol Rep* 2015;16:32.
46. Ahmed K, Khan SA, Hayn MH, Agarwal PK, Badani KK, Balbay MD, *et al.* Analysis of intracorporeal compared with extracorporeal urinary diversion after robot-assisted radical cystectomy: Results from the International Robotic Cystectomy Consortium. *Eur Urol* 2014;65:340-7.
47. Patel HR, Santos PB, de Oliveira MC, Müller S. Is robotic-assisted radical cystectomy (RARC) with intracorporeal diversion becoming the new gold standard of care? *World J Urol* 2016;34:25-32.
48. Khan MS, Gan C, Ahmed K, Ismail AF, Watkins J, Summers JA, *et al.* A single-centre early phase randomised controlled three-arm trial of open, robotic, and laparoscopic radical cystectomy (CORAL). *Eur Urol* 2016;69:613-21.
49. Winters BR, Bremjit PJ, Gore JL, Lin DW, Ellis WJ, Dalkin BL, *et al.* Preliminary comparative effectiveness of robotic versus open radical cystectomy in elderly patients. *J Endourol* 2016;30:212-7.
50. Messer JC, Punnen S, Fitzgerald J, Svatek R, Parekh DJ. Health-related quality of life from a prospective randomised clinical trial of robot-assisted laparoscopic vs open radical cystectomy. *BJU Int* 2014;114:896-902.
51. Smith ND, Castle EP, Gonzalgo ML, Svatek RS, Weizer AZ, Montgomery JS, *et al.* The RAZOR (randomized open vs robotic cystectomy) trial: Study design and trial update. *BJU Int* 2015;115:198-205.
52. Chan KG, Guru K, Wiklund P, Catto J, Yuh B, Novara G, *et al.* Robot-assisted radical cystectomy and urinary diversion: Technical recommendations from the Pasadena Consensus Panel. *Eur Urol* 2015;67:423-31.
53. Azhar RA, Bochner B, Catto J, Goh AC, Kelly J, Patel HD, *et al.* Enhanced recovery after urological surgery: A contemporary systematic review of outcomes, key elements, and research needs. *Eur Urol* 2016;70:176-87.
54. Deibert CM, Silva MV, RoyChoudhury A, McKiernan JM, Scherr DS, Seres D, *et al.* A prospective randomized trial of the effects of early enteral feeding after radical cystectomy. *Urology* 2016;96:69-73.
55. Matulewicz RS, Brennan J, Pruthi RS, Kundu SD, Gonzalez CM, Meeks JJ. Radical cystectomy perioperative care redesign. *Urology* 2015;86:1076-86.
56. Wuethrich PY, Burkhard FC. New perioperative fluid and pharmacologic management protocol results in reduced blood loss, faster return of bowel function, and overall recovery. *Curr Urol Rep* 2015;16:17.
57. Wuethrich PY, Studer UE, Thalmann GN, Burkhard FC. 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 randomised trial. *Eur Urol* 2014;66:352-60.
58. Burkhard FC, Studer UE, Wuethrich PY. Superior functional outcome after radical cystectomy and orthotopic bladder substitution with restrictive intraoperative fluid management: A followup study of a randomized clinical trial. *J Urol* 2015;193:173-8.
59. Baack 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 Oncol* 2016;34:120.e17-21.

How to cite this article: Kukreja JB, Shah JB. Advances in surgical management of muscle invasive bladder cancer. *Indian J Urol* 2017;33:106-10.