

Is Open Radical Cystectomy Facing Extinction?

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Open radical cystectomy with variety of urinary diversions has remained the gold standard for the treatment of muscle invasive bladder cancer. This is a major surgical procedure with significant post-operative morbidity and mortality.

Over the last decade laparoscopy and robotics have made significant inroads into our surgical practice. The well known attractions of minimally invasive surgery include reduced blood and tissue fluid loss during surgery, less post-operative pain, shorter hospital stay, quicker return to work, cosmetically pleasing results and equivalent cancer control.

The difficulty in widespread adoption of these minimally invasive options are steep learning curves, limited facilities for training, in the case of robotics formidable initial capital costs and cost of disposables. At present it may be fair to say that there is still a place for open, laparoscopic and robotic radical cystectomy until we have made rigorous evaluation of the new minimally invasive surgical options. A review of our experience of minimally invasive radical cystectomy will be presented.

Key words: laparoscopic radical cystectomy, radical cystectomy, robotic radical cystectomy

INTRODUCTION

Bladder cancer is the fourth most common cancer in men accounting for 5.5% of all cancer cases. Amongst women it is the 8th most common cancer accounting for 2.3% of all cancers (1). Bladder tumours exhibit a wide spectrum of biologic aggressiveness from benign behaving superficial low-grade papillary neoplasms to highly malignant anaplastic carcinomas.

Superficial bladder cancer represents nearly 75% of the bladder tumours at first presentation. It comprises a hetero-genous group of tumours that do not invade the muscularis propria. Majority of these patients can be managed by transurethral resection with or without intra-vesical chemo or immunotherapy. The overall 5 year survival rate of these patients is 70%- most patients dying from non-bladder cancer causes (2).

A certain proportion of patients with superficial bladder cancer progress to muscle invasion. High-grade T1 tumours (G3 pT1) have 30-50% risk of progression (3). Likewise carcinoma in situ (CIS) either alone or in association with papillary tumours have potential to develop into a muscle invasive disease in 20-80% of cases (4). About 25% patients with newly diagnosed bladder cancer have muscle invasive disease at presentation and vast majority of these are of poor histological differentiation.

Radical cystectomy remains the best therapy for invasive and regional bladder cancer, high-risk superficial tumours resistant to intra-vesical therapy, carcinoma-in-situ resistant to intra-vesical immuno or chemotherapy and recurrent multi-focal superficial disease refractory to repeat trans-urethral resection with/without intra-vesical therapy.

Open radical cystectomy (ORC) has been the standard of care. Initial reports of laparoscopic radical cystectomy (LRC) started emerging in 1995 with various forms of urinary diversions including cutaneous (ileal conduit, ureterostomy), continent

(Mainz II) and orthotopic urinary diversions as alternatives to open surgery. This was followed by reports of robotic radical cystectomy (RRC) and a variety of urinary diversions.

Advantages of the minimally invasive radical cystectomy (MIRC) include reduced blood and fluid loss, less post-operative pain, shorter hospital stay, quicker return to normal activity, cosmetically better outcome and equivalent cancer control in the short-term. The main disadvantages of MIRC are the steep learning curve, longer operating times and higher costs.

Open Radical Cystectomy (ORC)

Open radical cystectomy (ORC) has been the mainstay of surgical treatment for muscle invasive tumours and selected cases of superficial bladder tumours as alluded to above. Many centres around the world with interest in bladder cancer management have performed thousands of these procedures with outcomes published in the urological literature. Refinement of surgical techniques, availability of ingenious devices like ligasure and harmonic scalpel and improvements in post-operative surgical care, have resulted in significant reduction in mortality and morbidity.

In spite of improvement in surgical techniques and reduction in mortality and morbidity ORC remains one of the most major surgical procedures performed by the urological surgeons. Even in the best centres the major complication rate is around 5% and minor complications occur in up to 30% patients. Open surgery entails longer incisions and prolonged period of surgical retraction. This renders the incision quite painful and patients require higher doses of opiates and other analgesics post-operatively. Excessive bowel handling and opiates lead to prolonged ileus, which is the most common complication after ORC. Prolonged exposure of the bowel causes excessive fluid loss during surgery. Blood loss during ORC remains high and approximately 25-50% patients require blood transfusion. Longer incisions result in

poor cosmetic result. Patients stay longer in the hospital. There is considerable delay in return to normal activity with consequent higher cost to the health care system and personal loss of earnings(5, 6).

Optimum standards in terms of surgical outcomes and number of cases per centre have been defined in ORC. The acceptable standards require no more than 10% positive surgical margins overall and 15% in patients with T3 & T4 tumours. The median number of lymph nodes removed should be 10-14. It is recommended that at least 10 cystectomies should be performed at any particular centre annually to maintain adequate levels of surgical competence (7).

Three risk factors make radical bladder surgery more challenging. These include relatively old age of patients, higher incidence of smoking related respiratory dysfunction and age related co-morbidities. Thus besides the complexity and magnitude of surgery higher prevalence of co-morbidities makes the management of this patient population quite challenging.

Laparoscopic Radical Cystectomy (LRC)

With increasing experience in laparoscopic surgery, urologists around the world have attempted increasingly complex laparoscopic surgical procedures. Laparoscopic radical cystectomy poses a unique surgical challenge, as it involves not only ablation of the diseased bladder but in addition reconstruction of urinary diversion. The latter part of the procedure is testing even for the most experienced and skilled laparoscopic surgeons.

Surgeons with different levels of surgical expertise have adopted three approaches to reconstruction. The most common is extra-corporeal reconstruction either through a mini-laparotomy or extension of one of the port sites. This incision also used for delivering the specimen and lymph nodes. As the incision is small and muscle splitting its morbidity is negligible. It does not compromise the advantages of MIRC to any significant extent. Others have used a combined approach whereby after extra-corporeal reconstruction of the reservoir, it is returned into the pelvic cavity and urethro-vesical anastomosis completed intra-corporeally under direct vision. The least common approach is complete intra-corporeal reconstruction and anastomosis.

LRC has been evolving over the last decade. The first laparoscopic cystectomy was a simple cystectomy performed in 1992 for pyocystis on a paraplegic lady who previously had undergone ileal conduit urinary diversion for intractable urinary incontinence (8). The procedure took 2 hours and 10 minutes. There were no intra or post-operative complications and patient was discharged after 5 days.

The first LRC was reported in 1995 by Sanchez de Badajoz et al. The patient was a 64 year old lady who had invasive bladder cancer (9). Puppo et al, reported a series of LRC with trans-vaginal delivery of specimens, in the same year. Ileal conduit in this series was fashioned through a mini-laparotomy. Total operating time ranged from 6-9 hours and hospital stay was 7-11 days (10).

Denewer et al reported (1999) a series 10 laparoscopic salvage (post-radiation) radical cystectomies and uretero-sigmoidostomy as urinary diversion through a mini-laparotomy. One of these

patients died due to uncontrolled reactionary haemorrhage. Other complications included injury to the external iliac artery, a urinary fistula, a pelvic collection and deep venous thrombosis (11).

Kozminski & Partamiam (1999) were the first to report reconstruction of an ileal conduit using combination of laparoscopic and extra-corporeal approaches. Mobilization of the ureters and transposition of the left ureter through the sigmoid mesocolon was accomplished laparoscopically. Bowel and uretero-ileal anastomoses were completed after extending the port site incisions (12).

LRC and complete intra-corporeal construction of an ileal was first reported by Gill et al in year 2000. (13,14). Turk et al (2001) subsequently reported LRC and intra-corporeal construction of a continent recto-sigmoid pouch in 5 patients (15). A further milestone in MIRC and construction of intra-corporeal orthotopic neo-bladder was achieved by Gill et al. (16).

Most reports of LRC with ileal conduit urinary diversion do not differ significantly with regard to the operating time and the type and frequency of post-operative complications. The operating time appears to be proportional to the experience of the surgeon. In most series surgeons were at the early phase of the learning curve with operating times usually in the range of 6-8 hours. However, in a recent series reported by Cathelineau et al the median operating time was very respectable at 4 hours 20 minutes (17). In our experience the operating time reduces with increasing experience and becomes equivalent to ORC. Therefore this factor can no longer be considered as a disadvantage of the LRC provided the operating surgeons have enough through put to maintain and improve the operating skills.

The longer operating times highlights the difficulties associated with the learning curve of this complex surgical procedure and in particular construction of urinary diversion. Although LRC and continent urinary diversions and orthotopic reconstruction of the bladder have been accomplished entirely intra-corporeally, operating times are fairly long. Therefore it is difficult to justify such a prolonged anaesthetic for the complete intra-corporeal approach.

Overall complication rate of LRC is around 12.6% with re-intervention rate of 2.3%. In most laparoscopic series time to resumption of oral intake ranges from 2-4 days and hospital stay 6-8 days. Gupta et al reported return to light work 4 weeks after a LRC and urinary diversion (18). However, in our experience 6 weeks is a more realistic achievable goal.

Our group has performed 38 radical cystectomies and ileal conduit urinary diversion using extra-corporeal approach through extension of the port site. Operating time ranged from 230-390 minutes. Mean blood loss was 212 mls (50-1200mls). There were no conversions. The number of lymph nodes harvested ranged from 11-36. There was one positive surgical margin. All patients made excellent recovery at 6 weeks.

Basillote et al compared LRC and ileal neo-bladder constructed through a 15 cm Pfannenstiel incision with ORC and ileal neobladder. This was a retrospective analysis of the results. He concluded, that laparoscopic assisted procedure is associated

with decreased post-operative pain and quicker recovery (19). Taylor et al reported a prospective non-randomized comparison of hand assisted laparoscopic (HAL) cystectomy (n=8) and ORC with ileal conduit diversion and concluded that HAL cystectomy is associated with less blood loss, decreased post operative analgesic requirements, quicker return of bowel function and shorter length of hospital stay (20).

Oncologic safety and effectiveness has been a concern of the laparoscopic surgery in particular the risk of port site recurrence. So far there are no reports of port site recurrences and surgical margins have been reported clear in all cases of LRC. As most surgeons have been operating on highly selected group of patients, some critics attribute these results to better patient selection. On the contrary proponents feel that better vision and precision offered by the laparoscopy gives better results.

Extended lymphadenectomy has been shown to have a positive impact on the long-term outcome of the radical cystectomy (21). One of the criticisms of laparoscopic cystectomy have been the inadequacy of lymphadenectomy due its technical difficulties and impact on the operating time. However, it is possible to achieve an extended lymphadenectomy laparoscopically, though this adds an additional hour to the operating time. There are two series of LRC reporting survival rates of 85% and 65% at 3 years. In one series survival is comparable to ORC (22), but other showing inferior results, attributed to poor histological differentiation of the treated cases (23).

Robotic Radical Cystectomy (RRC)

There are certain inherent disadvantages of laparoscopic surgery. These include relatively long instruments inserted through the fixed entry points. There is an unnatural hand to eye co-ordination and often loss of eye-hand target axis during the procedure. Visual depth perception is poor because of two-dimensional view. Surgeon is dependent on the assistant to hold the camera and hence the view of the surgical field is not under surgeon's control. Most importantly surgical procedures like cystectomy are physically demanding and result in considerable surgeon's fatigue.

Robotic assistance allows hand to eye alignment, navigator camera control and stereoscopic vision providing an open surgical orientation. Other advantages include 7 degrees of freedom of movement of the instruments, ambidextrous capability and elimination of tremors. Da Vinci has open architecture and can allow motion scaling. Thus benefits to the surgeon include improved dexterity, enhanced visualisation, greater surgical precision, increased range and intuitiveness of motion, improved access and reduced fatigue. Hence robotic assistance translates open surgery into minimally invasive surgery. The advent of robotic surgery may be particularly useful in the construction of urinary reservoirs. The main drawbacks of robotics are the costs of implementation and lack of haptic feedback.

RRC and urinary diversion, was first reported by Menon et al in 2003 (24). Similar to LRC, it involves a six port trans-peritoneal approach but focuses on the initial development of the recto-vesical plane prior to transecting the recto-vesical pedicles. The procedure was performed in three stages; firstly pelvic lymphadenectomy and cystoprostatectomy, secondly extracorporeal

formation of a neobladder and thirdly intra-corporeal urethro-neovesical anastomosis following re-docking of the robot. The operative times ranged from 260-310 minutes depending on whether an ileal conduit or orthotopic neobladder was formed. Blood loss was <150mls and margins were clear in all cases.

Two further case series of 1 and 2 patients were reported in the same year. Beeken et al described formation of a Hautmann orthotopic neobladder intra-corporeally using a Da Vinci system with an operating time of 8.5 hours and a blood loss of 200 ml. (25). Balaji's group from Nebraska performed a robotic-assisted totally intracorporeal laparoscopic ileal conduit urinary diversion (26). The latter on 2 men and 1 woman had an operative time of 630-830 minutes with a hospital stay of 5-10 days. They highlighted the need for further operative refinement to reduce rather lengthy operative time. The operative times for urinary diversion ranged from 260-310 minutes depending on whether an ileal conduit or orthotopic neobladder was formed. Blood loss was <150mls and margins were clear in all cases.

The Guy's technique of RRC and ileal conduit diversion has evolved from the Vattikuti RRC (24) and Eastbourne LRC (27). A team of surgeons experienced in robotic, laparoscopic and open radical cystectomy participate in each procedure. Posterior and lateral dissections are performed first with anterior dissection and control of the dorsal venous plexus left to the end. Ileal conduit formation is performed through a midline or appendix incision. Blood loss is on average 150 ml with hospital stay of 11 days. There have been no deaths so far. Patients over 60 are given prophylactic digoxin to prevent post-operative cardiac arrhythmias. All oncological margins are negative and at 1 year follow-up no recurrences or metastases have occurred.

CONCLUSION

LRC and RRC offer the advantages of minimally invasive surgery with better or at least equivalent outcomes in terms of cancer control. Operating times at present are expectedly long but there is an obvious trend in improvement with increasing experience. In view of the complexity of the procedure, it is best performed by a team of surgeons with advanced expertise in MIRC. This will allow pooling of the cases in major centres, and shorten the learning curve. Once long-term oncologic and functional results become available, MIRC is likely to become the standard of care in all age groups. Nerve and prostate sparing MIRC are achievable and offer younger patients the possibility of maintaining potency.

Having established the feasibility, safety and short-term effectiveness of the MIRC, the time is right for randomised comparative trials with ORC. The parameters to be compared should include patient's age, co-morbidities/ASA grade, stage and grade of the tumour, extent of lymph-adenectomy and number of lymph nodes retrieved, operating time, blood loss, need for transfusion intra or post-operatively, analgesic requirement (opiates and non-opiates), length of paralytic ileus, time to mobilisation, hospital stay, time to return to normal activity, health related quality of life (HRQL) assessment using standard instruments, minor and major complications, costs of treatment and follow up of up to 5 years. Until such trial data are available it would be fair to say that there is still a place for open, laparoscopic and robotic radical cystectomy.

TABLE 1
 Outcomes of MIRC
 TABLICA 1.
 Ishodi MIRC-a

Authors/ Autori	Reconstruction/ Rekonstrukcija	N	Estimated blood loss, litres/ Predvideni gubitak krvi, u litrama	Operative time, hr/ Trajanje operacije, u satima	Operative margins/ Kirurški rubovi	Complications/ Komplikacije
Puppo (6) 1995	IC Extra-corporeal/ izvan tijela	5	3 transfused 2- 6 units/ 3 puta tranfuzirano 2- 6 jedinica	6-9	NS	none/nikakve
Denewer (7) 1999	MU Extra-corporeal/ izvan tijela	10	2.2 units (2-3)/ 2.2 jedinice (2-3)	3.6 (3.2- 4.1)	NS	1 x death (bleeding)/smrt (krvarenje) 1 x external iliac artery clipped/ klemana vanjska ilijačna arterija 1 x urine leak/curenje urina, 1 x DVT 1 x pelvic collection/nakupine u zdjelici
Gill (9) 2000	IC Intra-corporeal/ unutar tijela	2	1.1 (1.0-1.2)	10.8 (10- 11.5)	All -ve/ Sve negativno	none/ nikakve
Gupta (25) 2002	IC Intra-corporeal/ unutar tijela	5	0.36 (0.3-0.4)	7.5 (7-8)	All -ve/ Sve negativno; 2 nodes+ve/ 2 čvora pozitivno	1 x bowel obstruction/ opstrukcija crijeva 1 x abdominal distension/ distenzija abdomena
Turk (11) 2001	MU Intra-corporeal/ unutar tijela	5	0.25 (0.19-0.3)	7.4 (6.9- 7.9)	All -ve/Sve negativno	none/ nikakve
Gill (12) 2002	OIN/IP Intra/Extra Unutar/Izvan	2/1	0.3/0.3	9.5/7	All -ve/Sve negativno	Bleeding duodenal ulcer/Krvareći čir na dvanaesniku
Hemal (26) 2003	IC Extra-corporeal/ izvan tijela	10	0.53	6.5	1/10 positive/ pozitivan	1 x open conversion/ konverzija na klasičnu otvorenu operaciju/postupak 5 major/minor 5 većih/manjih komplikacija
Menon (18) 2003	OIN/IC Extra-corporeal/ izvan tijela Robot assist/ uz pomoć robota	17	<0.15	5.1/4.3	All -ve/Sve negativno	1 x open exploration for bleeding/ otvorena eksploracija zbog krvarenja. 1 x conversion for optic problem/ konverzija zbog problema s optikom
Cathelineau (27) 2005	33 IC 51 OIN Extra-corporeal/ izvan tijela	84	0.5 (0.15-2.0)	4.7 (3.6- 5.5)	All -ve/Sve negativno	2 x urinary fistulas/ urinarne fistule 3 x haematomas/ hematoma 1 x pyelonephritis/ pijelonefritis 1 x PE 8 x urinary infections/ urinarne infekcije
DeGer (16) 2004	OIN/IC/MU 5/3/12 Intra-corporeal/ unutar tijela	20	0.2 (0.19-0.8)	8.1 (6.1- 13.8)	All -ve/Sve negativno; 3 lymph nodes+ve/ 3 limfna čvora pozitivna	1 x persistent leakage of the pouch/ perzistirajuće curenje pouch-a 1 x rectovaginal fistula/ rektovaginalna fistula both needed re-operation/ u oba slučaja bila je nužna reoperacija

Yang (28) 2005	IC HA 11/ Lap 7	18	286/179	6.5/6.0	NS	no major complications/ bez većih komplikacija
Simonato (17) 2005	OIN/US/CU 6/2/2 Extra-corporeal/ izvan tijela	10	0.31 (0.2- 0.40)	9.8 (8.5- 10.5)	All -ve/Sve negativno	
Huang (29) 2005	Orthotopic neobladder/ Ortotopični neomjehur Extra-corporeal/ izvan tijela	33	0.46 mean/ prosječno 0.46	6.5 hours/ 6.5 sati	All -ve/Sve negativno	6/33 (18%) 2 x pouch leakage/curenje iz pouch-a 2 x bowel obstruction/opstrukcija crijeva 1 x fistula 1 x pelvic infection/1 x zdjelična infekcija

Abbreviations (TABLE 1): IC: Ileal Conduit, MU: modified ureterosigmoidostomy, OIN: Orthotopic Ileal neobladder, IP: Indiana Pouch, CU: Cutaneous urostomy, US: Ureterosigmoidostomy, HA: hand-assisted, PE: pulmonary embolism, DVT: Deep vein thrombosis, NS: not stated

Skraćenice (TABLICA 1.): IC: ilealni conduit, MU: modificirana ureterosigmoidostomija, OIN: ortotopični ilealni neomjehur, IP: Indiana Pouch, CU: kutana urostomija, US: ureterosigmoidostomija, HA: ručno potpomognut/a, PE: plućna embolija, DVT: duboka venska tromboza, NS: nije navedeno

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PRIJETI LI "IZUMIRANJE" OTVORENOJ RADIKALNOJ CISTEKTOMIJI?

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SAŽETAK

Otvorena radikalna cistektomija sa svim pridruženim oblicima derivacije urina je zlatni standard u liječenju invazivnog raka mokraćnog mjehura. Radikalna cistektomija je opsežna operacija sa značajnim poslijeoperacijskim morbiditetom i smrtnošću.

Tijekom proteklog desetljeća, laparoskopija i robotika značajno prodiru u svakodnevnu kiruršku praksu. Općenito prihvaćene prednosti minimalno invazivne kirurgije uključuju smanjeni operativni gubitak krvi i tjelesnih tekućina, slabiju poslijeoperacijsku bol, kraći bolnički boravak, brži povratak radnim aktivnostima, estetski ugodne rezultate i zadovoljavajuću kontrolu maligne bolesti.

Poteškoće u širem prihvaćanju minimalno invazivnih operacija jesu strma krivulja učenja, ograničen broj centara za edukaciju, a u slučaju robotski potpomognute kirurgije veliki početni trošak i trošak potrošnih materijala. Za sada u našoj svakodnevnici ima mjesta za otvorenu, laparaskopsku i robotski potpomognutu radikalnu cistektomiju, sve dok se ne učini temeljita procjena i usporedba novih minimalno invazivnih kirurških opcija. Prikazat ćemo pregled naših iskustava u minimalno invazivnoj radikalnoj cistektomiji.

Ključne riječi: laparaskopska radikalna cistektomija, radikalna cistektomija, radikalna cistektomija potpomognuta robotikom