

Robot-assisted Radical Cystectomy with Intracorporeal Urinary Diversion following Neoadjuvant Chemotherapy for Muscle-invasive Bladder Cancer: An Initial Experience

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What's known on the subject? and What does the study add?

Robot-assisted techniques are frequently used in oncological surgeries. As these techniques achieve oncological and functional results comparable to open surgical approaches over time, the advantages of the laparoscopic approach can be provided to patients during recovery. The contribution of neoadjuvant chemotherapy to survival in the muscle-invasive bladder cancer patient group has been reported in the literature. In this study, we aimed to share our intracorporeal urinary diversion results, which may be technically challenging, in the patient group who received neoadjuvant chemotherapy.

Abstract

Objective: To investigate the outcomes of robot-assisted radical cystectomy, intracorporeal urinary diversion, and extended lymph node dissection in patients with muscle-invasive bladder cancer who underwent neoadjuvant chemotherapy.

Materials and Methods: A total of 14 patients underwent neoadjuvant chemotherapy for invasive bladder tumors, followed by robot-assisted radical cystectomy, extended lymph node dissection, and intracorporeal urinary diversion. Demographic, operative, and postoperative information of the patients was retrospectively evaluated. Gemcitabine plus cisplatin and cisplatin plus etoposide regimens were used as neoadjuvant treatments. Early and late-term complications were recorded.

Results: In the early postoperative period (0–30 days), Clavien-Dindo grade 2 complications occurred in 6 patients and grade 3 complications in 2 patients. In the late postoperative period (31–90 days), Clavien-Dindo grade 2 complications occurred in 1 patient and grade 3 complications in 1 patient. The mean follow-up period was 15.5±5.7 months.

Conclusion: Although the intracorporeal technique is more demanding in terms of learning and use, preoperative chemotherapy application should not be seen as a limitation in the application of this technique.

Keywords: Bladder cancer, neoadjuvant chemotherapy, radical cystectomy, reconstructive urology, robot-assisted surgery, urinary diversion, urooncology

Introduction

Bladder cancer diagnosis ranks second among urological cancers (1). A quarter of these cancers are detected in the muscle-invasive stage (2). The gold standard treatment for muscle-invasive bladder cancer is radical cystectomy and lymph

node dissection, with neoadjuvant chemotherapy also applied in suitable patients (3).

Radical cystectomy can be performed classically as open, laparoscopic, or robot-assisted. The increasing approval of robotic surgery in recent years, and its comparable success

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with open surgery in oncological and functional outcomes, particularly in kidney and prostate cancer, brings the applicability of this approach to radical cystectomy as well (4,5). In recent years, radical cystectomy has been performed mostly with robot assistance, especially in clinics that perform high-volume surgery (6). With the minimally invasive approach provided by robotic surgery, it is intended to reduce perioperative fluid loss, blood loss, pain, normalization of bowel movements in a shorter time, and hospital stay. In addition, executing the urinary diversion intracorporeally, which is an important step of the surgery, will exploit these advantages (7,8). Evidently, the oncological and functional results of the robot-assisted approach should not be inferior to those of open surgery. Series on this topic demonstrate the efficacy and feasibility of this treatment approach (4,5).

Studies have shown the survival advantage of neoadjuvant chemotherapy before radical cystectomys (9-12). Therefore, neoadjuvant chemotherapy is being applied more frequently in patients who are suitable for chemotherapy. Although there is an outlook that neoadjuvant chemotherapy will cause additional perioperative complications for a morbid operation such as radical cystectomy, there are important studies contrary to this template (7,13). Furthermore, the manner in which urinary diversion is performed after radical cystectomy is another issue.

In this study, we aimed to share the outcomes of robot-assisted radical cystectomy, intracorporeal urinary diversion, and extended lymph node dissection in 14 patients with

muscle-invasive bladder cancer who underwent neoadjuvant chemotherapy.

Materials and Methods

Between February 2018 and June 2022, 14 patients underwent neoadjuvant chemotherapy for invasive bladder tumors followed by robot-assisted radical cystectomy, extended lymph node dissection, and intracorporeal urinary diversion using the DaVinci Surgical System Xi (Intuitive Surgical Inc., Sunnyvale, CA, USA). Demographic, operative, and postoperative information of the patients were evaluated (Table 1). The chemotherapy regimen was gemcitabine plus cisplatin combination for 13 patients and cisplatin plus etoposide combination for 1 patient. All patients were evaluated after the second cycle to determine the response to chemotherapy. For all 14 patients, after 2 cycles, evaluation consisted of radiologically stable or remission disease. At this point, it is decided to complete four cycles of chemotherapy for all patients. During the chemotherapy, there were no major complications that may indicate discontinuation of treatment or that prevented surgery.

Surgical technique: The surgical technique of robotic radical cystectomy and lymph node dissection has been described in detail in many previous studies (14-16). The steps for intracorporeal urinary diversion continue as follows: Preparation of the left ureter and its route to the right in a retromesenteric opening, followed by 25 mg of indocyanine green mixed with

Age (year ± SD)	66±7.6		
ASA	2: 14 (100%)		
BMI	30.3±3.7		
Sex	M: 11 (78.5%) F: 3 (21.5%)		
Preoperative T stage (n, %)	T1: 2 (14%) T2: 10 (71%) T3: 1 (7%) T4: 1 (7%)		
Concomitant CIS	Yes: 6 (43%) No: 8 (57%)		
Operation time (min ± SD)	295±137	278±140 (IC)	311±110 (ON)
Estimated blood loss (mL ± SD)	280±86	260±92 (IC)	288±77 (ON)
Length of stay (days ± SD)	6.7±1.6	6.5±1.5 (IC)	6.9±1.7 (ON)
Ileal orthotopic neobladder (n, %)	7 (50%)		
Ileal conduit (n, %)	7 (50%)		
Postoperative pathologic t stage (n, %)	8 (57%) pT0 1 (7%) pT1	1 (7%) pT2	4 (28%) pT3
Lymph Nodes dissected (n ± SD)	22.6±12.6	21±13 (IC)	23±11 (ON)
Positive lymph node (n, %)	2 (14%)	1 (7%) (IC)	1 (7%) (ON)

IC: Ileal conduit, ON: Orthotopic neobladder, SD: Standard deviation, BMI: Body mass index

10 mL of distilled water, and 2 mL of this solution was injected intravenously just before spatulation and construction of the ureteroenteric anastomosis, following isolation and preparation of the ileal conduit or neobladder. For the intracorporeal neobladder, the steps defined by Wiklund and Poulakis (17) were performed. We verified the vascularity of the ureters with the intraoperative near-infrared fluorescence imaging system at the pre-anastomotic stage. Furthermore, the vascularity of the intestinal anastomosis and neobladder itself was controlled. Subsequently, healthy vascularized distal ureters were spatulate, and tension-free modified Wallace anastomoses were made over 6F single J stents using Stratafix 4/0 sutures. In patients in whom an ileal conduit was planned, the left ureter was passed to the right from the posterior of the sigmoid mesentery. A segment from the terminal ileum was isolated along with its mesentery, and ileo-ileal anastomosis was performed. Ureteroileal anastomosis was performed in the Wallace style. We also performed frozen section examinations of both distal ureters. Single J stents are maintained for 10 days for both the ileal conduit and neobladder.

Statistical Analysis

Data about the patients were collected and evaluated retrospectively. These included demographic information, clinical stage, perioperative information, and postoperative pathology. The complication rates were analyzed for the early (30 days) and late (30–90 days) periods, according to the Clavien–Dindo classification system (18). Ethics committee approval was obtained for the study (approval number: 2022-19/02, date: 09.12.2022 - Acbadem University Ethics Committee).

Results

The mean patient age was 66 ± 7.6 years. Mean operative time, intraoperative blood loss, and hospital stay were 295 ± 137 mins, 280 ± 86 mls and 6.7 ± 1.6 days, respectively. Urinary diversion was performed as an orthotopic neobladder in 7 (50%) patients

and as an ileal loop in 7 (50%) patients. The postoperative pathological stage was reported as pT0 in 8 (57%) patients, pT1 in 1 (7%) patient, pT2 in 1 (7%) patient, and pT3 in 54 (28%) patients. The mean number of lymph nodes removed in lymph node dissection was 22.6 ± 12 . Lymph node positivity was reported in the final pathology in 2 (14%) patients.

In the early postoperative period (0–30 days), Clavien–Dindo Grade 2 complications occurred in 6 (42%) and Grade 3 complications in 2 (14%) patients. In the late postoperative period (31–90 days), Clavien–Dindo Grade 2 complications occurred in 1 (0.7%) and Grade 3 complications in 1 (0.7%) patient (Table 2). The mean follow-up period was 15.5 ± 5.7 months. In patients who underwent neobladder urinary diversion, no voiding problems requiring catheterization were observed during the postoperative follow-up period, and no incontinence was detected.

Discussion

There are several studies in the literature that consider the effects of chemotherapy on the results of surgery. Predictions that chemotherapy may impact the results of surgery, including delayed wound healing and liability for infections. In addition, it is thought that hematological side effects such as neutropenia and thrombocytopenia due to chemotherapy may be effective in the early postoperative period. Radical cystectomy is one of the most morbid surgeries in urology and typically needs to be performed when the patient is in the fittest condition. However, because of the aggressive nature of the disease, sometimes there may not be an opportunity to wait for the fittest condition of the patients. These patients, who often have additional morbidities such as chronic obstructive pulmonary disease due to advanced age and smoking, can be operated on after chemotherapy to obtain the possible survival advantage of neoadjuvant chemotherapy, as mentioned in the literature (10). It is important that tissue healing is adequate for ureteral and intestinal anastomoses, which is an important step of urinary diversion.

Table 2. Post-operative complications (Clavien–Dindo classification)

	Postoperative period (0–30 days)	Postoperative period (31–90 days)
Clavien–Dindo grade 2 (n)	Urinary tract infection (5) (35%) (2 IC, 1 ON) Ileus (1) (0.7%) (1 ON)	Urinary tract infection (1) (0.7%) (ON)
Clavien–Dindo grade 3a (n)	Repositioning of neobladder catheter under local anesthesia (1) (0.7%) (ON)	-
Clavien–Dindo grade 3b (n)	Removing of an intraabdominal part of the draining catheter under general anesthesia (1) (0.7%) (IC)	Parastomal hernia repair (1) (0.7%) (IL)
Follow-up (months)	15.5±5.7	

IC: Ileal conduit, ON: Orthotopic neobladder

The second main subheading in our study regarding the treatment of this patient group is the step of performing urinary diversion intracorporeally. There are significant expected benefits of performing this morbid surgery laparoscopically: less pain, therefore less use of painkillers, earlier onset of bowel movements and earlier oral nourishment, shortening of the duration of hospitalization, and therefore less risk of hospitalization-related complications with an expectation of earlier return to daily life.

Of course, performing the even more subtle urinary anastomosis phase of this delicate surgery intracorporeally may take a long learning curve. Consequently, we recommend a selective approach, focusing on surgeons' experience and cautiously assessing patient-based factors.

Studies in the literature report early-term complication rates for radical cystectomy between 20% and 40% and late-term complication rates between 11% and 20% (19–21).

In the study by Nguyen et al. (13), published in 2018, in which they presented data on 40 patients, the early and late complication rates after radical cystectomy in patients receiving neoadjuvant chemotherapy were 35% and 12.5%, respectively. Reported early complications include urinary tract infection, hemorrhage, urine leakage, acute renal failure, lymphocele, and pulmonary embolism. Late complications include urinary tract infection, ileus, and acute renal failure. Two of the patients died due to intestinal obstruction and sepsis (13). These rates are comparable with the complication rates in radical cystectomy series that did not receive neoadjuvant chemotherapy.

The early-term complication rate for our patient group seems high at 57% (8/14), but these complications generally present as infections that are controlled with appropriate antibiotic therapy. In the higher Clavien-Dindo group, complications included one patient requiring intervention under general anesthesia because of a retained drain fragment in the abdomen and another patient necessitating reinsertion of the 22 F Foley catheter under local anesthesia (lidocaine 2% gel) due to its dislodgement.

Study Limitations

Noticeably, the small number of patients in our study is a limitation in the generalizability of the results. Additionally, there is a high possibility of patient selection bias in terms of the interpretation of retrospectively presented information. Nevertheless, we believe that our findings are encouraging in terms of the feasibility of robotic radical cystectomy, intracorporeal diversion, and extended lymph node dissection in patients receiving neoadjuvant chemotherapy.

It is quite possible to achieve a balance between the benefits of chemotherapy and its effects on surgery for the benefit of the

patient. Of course, at this stage, a multidisciplinary approach is required, in which the evaluation of anesthesiologists as well as oncologists and urologists is at the forefront.

Conclusion

There are benefits and drawbacks to intracorporeal or extracorporeal urinary diversion during robot-assisted radical cystectomy. When determining the technique, the surgeons' experience and patient factors should be considered. Although the intracorporeal technique is more demanding in terms of learning and application, it may provide the benefits of the laparoscopic approach. Preoperative chemotherapy application should not be seen as a limitation in the application of these techniques.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained for the study (approval number: 2022–19/02, date: 09.12.2022 – Acıbadem University Ethics Committee).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: T.D., Ö.B.A., M.B.T., İ.T., C.Ö., A.R.K., Concept: T.D., Ö.B.A., Design: T.D., Ö.B.A., Data Collection or Processing: T.D., Ö.B.A., Analysis or Interpretation: T.D., Ö.B.A., M.B.T., İ.T., C.Ö., A.R.K., Literature Search: T.D., Writing: T.D., Ö.B.A.

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