Radical Cystectomy after Previous Radiation or Pelvic Surgery: Is It Associated with Increased Morbidity?

Roy Croock MD, Jonathan Modai MD, Yuval Avda MD, Igal Shpunt MD, Yaniv Shilo MD, Yamit Peretz MD, Uri Lindner MD, Avraham Bercovich MD, and Dan Leibovici MD

Department of Urology, Kaplan Medical Center, Rehovot, Israel

ABSTRACT **Background:** Radical cystectomy is a complicated surgery with significant risks. Complications of Clavien–Dindo grade 3–4 range from 25% to 40% while risk of mortality is 2%. Pelvic surgery or radiotherapy prior to radical cystectomy increases the challenges of this surgery.

Objectives: To assess whether radical cystectomy performed in patients with prior history of pelvic surgery or radiation was associated with increased frequency of Clavien–Dindo grade 3 or higher complications compared to patients without prior pelvic intervention.

Methods: We retrospectively evaluated all patients who underwent radical cystectomy at our center over a 7-year period. All patients with pelvic radiation or surgery prior to radical cystectomy comprised group 1, while group 2 included the remaining patients.

Results: In our study, 65 patients required radical cystectomy at our institution during the study period. Group 1 was comprised of 17 patients and group 2 included 48 patients. Four patients from group 2 received orthotopic neobladder, while an ileal conduit procedure was performed in the remaining patients. Estimated blood loss and the amount of blood transfusions given was the only variable found to be statistically different between the two groups. One patient from group 1 had four pelvic interventions prior to surgery, and her cystectomy was aborted.

Conclusions: Radical cystectomy may be safely performed in patients with a history of pelvic radiotherapy or surgery, with complication rates similar to those of non-irradiated or operated pelvises.

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KEY WORDS: morbidity, pelvic radiation, pelvic surgery, radical cystectomy

Radical cystectomy is the standard surgical procedure for muscle invasive bladder cancer (MIBC). The surgery includes complete resection of the entire urinary bladder, distal ureters, prostate, seminal vesicles and vas deferens in men; and resection of the bladder, uterus, and adnexa and part of the anterior vaginal wall in women. In addition, pelvic lymph node dissection is performed, which includes the removal of all fatty and lymphatic tissue from the obturator fossa along the external, internal, and common iliac vessels, and in the pre-sacral area. Surgical removal of the urinary bladder requires urinary diversion to allow adequate urine evacuation thereafter. This part of the operation typically includes either formation of an ileal conduit to the abdominal wall or of an orthotopic neobladder, or creation of a continent urinary diversion. This elaborate and complex surgery is associated with morbidity and mortality consistently reported to be 40% [1] and 2–3% [2-6], respectively.

Any surgery is more difficult and demanding when performed in a previously operated anatomic field or after radiation therapy. This result is due to enhanced fibrosis and scarring, which obliterates surgical planes and renders separation of tissues and organs from one another difficult and hazardous. Despite these risks, it is less clear whether such difficulties are necessarily translated to a higher rate of adverse events. Understanding whether previous surgical or radiation interventions to the pelvis increase the morbidity associated with radical cystectomy is important in planning this surgery and may play a role in patient advising and obtaining an adequate informed consent.

PATIENTS AND METHODS

We retrospectively reviewed medical charts of all patients who underwent radical cystectomy between January 2014 and June 2020. This patient group was divided into two subgroups: those who underwent prior pelvic surgery or radiation and those who did not. Clinical and demographic data, indications for surgery, and final pathology from surgery were all collected from the medical records. Surgery duration, the number of blood transfusions, and hospital stay duration were recorded.

Complications were defined as any deviation from a flawless intraoperative and postoperative course. All complications were abstracted from the medical charts and were graded according to the Clavien–Dindo grading system [7]. Complications grade ≥ 3, during surgery and in the first 30 days postoperatively as well as the number of readmissions and secondary invasive interventions were compared between the two groups within three months from discharge from hospital.

We used Student's *t*-test and chi-square to compare continuous and categorical variables, respectively, with a $P < 0.05$ considered as significant.

RESULTS

A total of 65 patients underwent radical cystectomy at our center during the study period. Group 1, with a history of previous intervention, consisted of 17 patients, while the remaining 48 patients comprised group 2. Clinical, demographic, and pathology data are presented in Table 1. Previous interventions among patients are listed in Table 2. All operations were performed using open surgery by two surgeons (DL and UL) with the assistance of residents and other staff. Urinary diversions consisted of ileal conduit in 59 patients and Studer type orthotopic neobladder in four patients. Non-orthotopic continent diversions were not conducted in any of the patients.

In our entire cohort of 65 patients, significanti bleeding necessitating blood transfusion occurred in 24 patients (37%) [Table 3]. Intraoperative complications occurred in 7 patients (11%), and delayed complications occurred in 22 patients (34%). Of the reported complications, 23 were grade 3–4 (38%), and two (3%) died of other causes: upper gastrointestinal bleed and sudden cardiac death.

The two patients did not undergo pelvic intervention prior to cystectomy. When comparing outcomes between the two groups, the only variable that was statistically different was the number of blood transfusions [Table 3]. Seven patients (41%) from group 1 and five (10%) from group 2 received at least two units of packed cells ($P = 0.008$). Surgery was aborted in one patient from group 1 due to massive abdominal adhesions from previous interventions. Abortion of her planned radical cystectomy meant inability to provide her with the optimal care for her cancer. Therefore we considered this a grade IV complication. In contrast, all of the patients in Group 2 completed surgery as planned.

Intraoperative complications of Clavien–Dindo ≥ 3 were observed in two cases from group 1 (10%) and three cases from group 2 (6%).

Postoperative complications of Clavien–Dindo ≥ 3 were observed in 4 patients from group 1 (23.5%) and 15 (31%) from Group 2. Invasive radiology or surgical interventions dating since discharge and until 3 months after surgery were observed in one patient from group 1 (6%) and eight patients from group 2 (17%). These differences were not found to be statistically significant. Six of the 14 patients with one prior intervention, and one of the three patients with multiple prior interventions experienced complications of Clavien–Dindo ≥ 3 ($P = 0.18$).

Forty of 65 patients (62%) had a completely uneventful surgery and postoperative recovery (Clavien–Dindo complications < 3) until discharge. Of them, 10 (58%) and 30 (63%) were Groups 1 and 2, respectively, $P = 0.21$ [Table 3].

Bladder cancer was the indication for surgery in all but one patient, who required a cystectomy due to radiation hemorrhagic cystitis with refractory bleeding. Pelvic lymph node dissection was performed in all surgeries completed for oncological purposes excluding one patient, whose surgery was aborted.

Table 1. Demographic, clinical, and pathology data on patients from both groups

Patients	Group 1 (n=17)	Group 2 (n=48)	*P* value
Sex			
Males	12 (71%)	42 (88%)	0.08
Females	5	6	
Median age, years (range)	72.1 (47–85)	68.7 45–85	0.18
Charlson Comorbidity Index			
≤ 3	3 (18%)	18 (38%)	0.08
4	5 (29%)	11 (23%)	
≥ 4	9 (53%)	19 (39%)	
Indication for surgery			
Muscle invasive bladder cancer	12 (71%)	40 (83%)	0.22
Early cystectomy for non-muscle invasive bladder cancer	4 (24%)	8 (17%)	
Radiation cystitis	1 (5%)	0	
Chemotherapy			
Neoadjuvant	3 (18%)	6 (13%)	0.14
Adjuvant	2 (12%)	10 (21%)	
None	12 (70%)	32 (66%)	
Urinary diversion type			
Ileal conduit	15*	44 (92%)	0.579
Neo bladder	–	4	
Average body mass index (range)	26.1 (19.5–39.8)	25.1 (18.9–33.5)	
Pathology bladder cancer			
T ≤ 2	7 (47%)	22 (46%)	0.16
T2N+	2 (13%)	9 (19%)	
T3–T4	6 (40%)	17 (35%)	
Total	15**	48	
Surgical margins			
Positive	0	1	
Negative	15	47	
Other cancer	–	1 (adenocarcinoma)	
Benign	1 (inflammatory changes)		

*one patient anephric, one procedure aborted
**one patient chronic inflammation, one procedure aborted

Table 2. Number and types of previous interventions in group 1

Patient	Number previous interventions	Intervention	Clavien–Dindo
I	1	EBRT	II
II	1	IH with mesh	II
III	1	SPP	I
IV	1	TURP	II
V	1	CS	II
VI	1	SPP	IIIB
VII	1	Colectomy	IV
VIII	1	EBRT	IIIB
IX	1	EBRT	II
X	1	SPP	IIIA
XI	1	Salpingectomy	IIIA
XII	1	PLND	I
XIII	1	IH	IIIB
XIV	1	TURP	II
XV	2	RPx, EBRT	II
XVI	3	RPx, bilateral IH with mesh	I
XVII	4	LAR, IH with mesh, ectopic pregnancy, EBRT	IV (aborted)

CS = cesarean section, EBRT = external beam radiotherapy, IH = inguinal hernia, LAR = low anterior resection, PLND = pelvic lymph node dissection, RPx = radical prostatectomy, SPP = suprapubic prostatectomy, TURP = transurethral resection of prostate

DISCUSSION

The ability to predict complication risks is important before embarking on any complex surgery. Better understanding and anticipations of certain risks may be advantageous in the preoperative planning stages and with patient selection. Patients may be better prepared to make informed decisions before a surgical procedure is undertaken. Previous operations and radiation therapy are both associated with scarring fibrosis and obliteration of natural anatomic planes. As a result, tissue dissection becomes more difficult and riskier during surgery [8]. Furthermore, tissue healing and repair may be hampered by previous intervention, which could lead to postoperative problems, perhaps less frequently encountered in the naïve patient. Therefore, from a surgeon`s perspective, performing surgery in a previously operated or irradiated field renders the procedure more difficult and more dangerous. We therefore anticipated that our two patient groups would be different with regard to perioperative morbidity with a more detrimental course in group1.

In our study, however, we have shown that among all variables assessed; only surgical bleeding was statistically different between the two patient groups.

The overall significant complications and mortality rates were consistent with those reported in the literature. In total, slightly more than a third of all of our patients experienced significant (grade ≥ 3) complications. Conversely, a total of 40 patients (62%) had an uneventful intraoperative and postoperative course, with no significant difference between the groups.

Contrary to our expectation, exposure to previous interventions was not translated into increased morbidity as complication rates in both groups seem similar overall. Importantly, one patient from group 1 did not complete the planned surgery (aborted), and unilateral pelvic lymph node dissection was performed in a second patient [Table 3],. Planned surgery was completed in all patients from group 2. Inability to complete the planned surgery, although uncommon, is a significant detrimental consequence of previous interventions that must be discussed with the patient while obtaining the informed consent. Adequate radical cystectomy in terms of margin status and extensiveness of lymph node dissection provides better outcome for patients with MIBC [9]. We therefore defined this case of aborted surgery as a grade 4 complication on the Clavien–Dindo scale. Our sample size was small and so, there was no clear trend for complication risk based on the number of previous interventions. In addition, our results represent the experience from a single center.

From the patient's perspective, our findings are encouraging in assuring that despite its complexity, radical cystectomy is relatively safe in most patients when performed by an experienced physician. Based on these results, urologists may feel safe to decide on radical cystectomy even in previously operated or radiated patients.

Previous studies have shown mixed results regarding postoperative morbidity in this patient subgroup. When considering minor complications (Clavien–Dindo I and II), Svatek and colleagues [10] showed no significant difference in postoperative ileus among those previously irradiated. However, Nguyen et al. [11] reported that PLND was omitted in 19% of patients with a history of radiation. Other studies have shown prior abdominal surgery and pelvic radiation to be an independent risk factor for high-grade complications [12,13]. Certain studies have demonstrated higher rates of uretero-ileal strictures and revision procedures [14,15], while others have shown no significant difference in such complications [13,16].

LIMITATIONS

This study included a small sample size from a single center. This sample size limited our ability to assess number of previous interventions as an independent risk factor for significant complications. However, the strength of our study demonstrates that complications from radical cystectomy after previous interventions are not different from the course experienced by patients who had not been exposed to previous interventions.

Table 3. Comparison of surgical complications and postoperative morbidity between groups 1 and 2

	Group 1 (N=17)	Group 2 (N=48)	*P* value
Blood transfusions (units)			
Intraoperative	6 (35%)	7 (15%)	0.055
1	2	3	
2	3	3	
3	1	1	
Postoperative	6 (35%)	5 (10%)	0.02
1	2	4	
2	3	1	
3	1	–	
Total	12 (70%)	12 (25%)	
Total number of patients requiring ≥ 2 units	7 (41%)	5 (10%)	0.008
Average estimated blood loss, ml, (range)	620 (200–1200)	558 (450–1900)	0.045
Clavien–Dindo			
≥ 3	7 (41%)	18 (37.5%)	0.23
3a	2	4	
3b	3	9	
IV	2*	3	
V	–	2	
IC surgery duration, mean minutes (range)	279.5 (223–430)	285 (181–446)	0.73
Studer pouch surgery duration, mean minutes (range)	NA	317 (244–376)	
Intraoperative complications	2 (12%)	3 (6%)	0.28
	1 vascular injury**	1 ischemia ileal anastomosis***	
	1 PLND unilateral only	2 violation of sigmoid ✸	

	Group 1 (N=17)	Group 2 (N=48)	*P* value
Postoperative complications	5 (29%)	15 (31%)	0.23
	1 vascular event ✸✸	4 acute abdomen ✲✲✲	
	1 parastomal abscess ✸✸✸	2 sepsis ⓄⓄ	
	1 entero-entero anastomosis leak✲	4 eventration ⓄⓄ	
	2 wound dehiscence✲✲	1 pelvic collection ⓄⓄⓄ	
		2hydronephrosis ⓄⓄⓄ	
		2 mortality	
Duration of hospitalization, mean days (range)	15.5 (6–32)	18 (7–35)	0.11
Postoperative ileus, mean days (range)	7.1 (4–18)	6.6 (3–19)	0.25
Patients requiring total parenteral nutrition	6 (35%)	13 (27%)	0.19
Uneventful operation, postoperative course (CD ≤ 2)	10 (59%)	30 (63%)	0.21
Readmission within 3 months	5 (29%)	22 (46%)	0.12
	2 febrile urinary tract infections	8 febrile urinary tract infections	
	1 surgical wound infection	8 abdominal pain	
	1 metastatic disease complications	1 cerebrovascular accident	
	1 acute renal failure	1 anemia	
		3 wound infection	
		1 vascular event	
Additional invasive procedures at 3 months	1 (6%)	8 (17%)	0.20
	1 palliative spinal surgery	3 nephrostomy	
	metastatic disease	3 collection drainage (IR)	
		1 fem-pop bypass	
		1 colostomy	

IC = ileal conduit

*1 aborted, **femoral-femoral bypass, ***revision of entero-entero anastomosis, ✸loop ileostomy, ✸✸Inferior vena cava filter insertion, ✸✸✸drain insertion by interventional radiology, ✲ileo-ileostomy revision, ✲✲closure of abdomen,✲✲✲exploratory laparotomy, ⓄIntensive care admission, ⓄⓄclosure of abdomen, ⓄⓄⓄper cutaneous nephrostomy

CONCLUSIONS

With the exception a higher rate of blood loss, radical cystectomies performed in previously operated or irradiated patients may be done safely without the risk of significant complications compared with the intervention naive patient.

Correspondence

Dr. R. Croock
Dept. of Urology, Kaplan Medical Center, Rehovot 76100, Israel
Phone: (972-8) 944-1642
Fax: (972-8) 944-1642
email: croock20@gmail.com

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Capsule

Physical rehabilitation for older patients hospitalized for heart failure

Kitzman and colleagues conducted a multicenter, randomized, controlled trial to evaluate a transitional, tailored, progressive rehabilitation intervention that included four physical-function domains (strength, balance, mobility, and endurance). The intervention was initiated during, or soon after, hospitalization for heart failure and was continued after discharge for 36 outpatient sessions. The primary outcome was the score on the Short Physical Performance Battery (total scores range from 0–12, with lower scores indicating more severe physical dysfunction) at 3 months. The secondary outcome was the 6-month rate of re-hospitalization for any cause. A total of 349 patients underwent randomization; 175 were assigned to the rehabilitation intervention and 174 to usual care (control). At baseline, patients in each group had markedly impaired physical function, and 97% were frail or pre-frail. The mean number of coexisting conditions was 5 in each group. Patient retention in the intervention group was 82%, and adherence to the intervention sessions was 67%. After adjustment for baseline Short Physical Performance Battery score and other baseline characteristics, the least-squares mean ± SE score on the Short Physical Performance Battery at 3 months was 8.3 ± 0.2 in the intervention group and 6.9 ± 0.2 in the control group (mean between-group difference, 1.5; 95% confidence interval [95%CI] 0.9–2.0; $P < 0.001$). At 6 months, the rates of re-hospitalization for any cause were 1.18 in the intervention group and 1.28 in the control group (rate ratio, 0.93; 95%CI 0.66–1.19). There were 21 deaths (15 from cardiovascular causes) in the intervention group and 16 deaths (8 from cardiovascular causes) in the control group. The rates of death from any cause were 0.13 and 0.10, respectively (rate ratio, 1.17; 95%CI 0.61–2.27).

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