



# Sexual Function after Non-Nerve-Sparing Radical Cystoprostatectomy: A Comparison between Ileal Conduit Urinary Diversion and Orthotopic Ileal Neobladder Substitution

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## ABSTRACT

**Objective:** To compare the erectile function (EF) and sexual desire (SD) in men after radical cystoprostatectomy (RCP) who had either an ileal conduit urinary diversion or orthotopic ileal neobladder substitution.

**Materials and Methods:** Eighty one sexually active men with bladder cancer were enrolled in this prospective study. After RCP according to patients' preferences they underwent either ileal conduit urinary diversion (n = 41) or orthotopic ileal neobladder substitution (n = 40). EF and SD were assessed using International Index of Erectile Function (IIEF) questionnaire. Patients were assessed at 4-week before surgery and were followed up at 1, 6, and 12-month postoperatively using the same questionnaire.

**Results:** Postoperatively the EF and SD domains deteriorated significantly in both groups, but in a small proportion of the patients submitted to ileal neobladder they gradually improved with time (P = 0.006). At 12-month postoperative period, 4 (9.8%) and 14 (35.0%) patients in ileal conduit and ileal neobladder groups were able to achieve erections hard enough for vaginal penetration and maintained their erection to completion of intercourse, respectively (P = 0.006). Among patients in the ileal conduit and ileal neobladder groups, additional 4 (9.8%) and 7 (17.1%) patients were able to get some erection, but were unable to maintain their erection to completion of intercourse (P = 0.02). At 12-month follow up period 24.4% of the ileal conduit and 45.0% of the ileal neobladder patients rated their sexual desire very high or high (P = 0.01).

**Conclusion:** When performed properly, orthotopic ileal neobladder substitution after RCP offers better long-term results in terms of EF and SD.

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## INTRODUCTION

Currently, radical cystoprostatectomy (RCP) is the standard procedure for aggressive superficial bladder cancer and locally confined

bladder carcinoma (1). Radical cystoprostatectomy with urinary diversion significantly affects patient's quality of life and sexual functioning. Reported recovery rate of erectile function (EF) after RCP was between 14%-80% (2-4). During

RCP neurovascular bundles are usually removed or severely damaged resulting in erectile dysfunction (ED). In patients with bladder cancer, the ileal conduit is still considered a standard form of urinary diversion following radical cystectomy (5). The main disadvantages are the presence of a stoma and external appliance, urinary leakage due to appliance problems and negative body image (6). In an attempt to overcome shortcomings with ileal conduit, continent cutaneous diversion and orthotopic bladder substitution were developed (7). It was assumed that these procedures would significantly improve the patient's quality of life. However, continent urinary diversions are criticized due to their technical difficulties and high early and late complication rates (8,9). But, Parekh et al. reported that, morbidity and mortality outcomes did not differ significantly between patients undergoing ileal conduit and orthotopic neobladder are comparable (10). In addition, many studies demonstrated that ileal conduit urinary diversion has equal health-related quality of life when compared with continent neobladder substitution (6,7,11). What remained unknown is the impact of these two methods of lower urinary tract reconstruction on sexual function. In the last decade, the issue of sexual function after RCP has been addressed in few studies. Hekal et al. (12) and Zippe et al. (3) reported that in a group of patients who underwent nerve sparing RCP the recovery of erectile function after surgery was better. In a review article, Park and Ahn concluded that orthotopic continent diversion provides good quality of life with few long-term complications (13). For the first time, in the present study we aimed to test whether there are differences between patients with an ileal conduit urinary diversion and those with orthotopic bladder substitution, in terms of EF and SD after RCP.

## MATERIALS AND METHODS

### Study population

During a five year period, between April 2006 and May 2010, a total of 206 patients with muscle invasive bladder transitional cell carcinoma (TCC) underwent radical cystoprostatectomy in study sites. Of these patients 102 met study criteria and

were recruited into the study. These men were sexually active and potent which were treated with RCP and urinary diversion. All participants underwent RCP with bilateral pelvic lymphadenectomy without attempting to nerve sparing surgery. Before surgery, all patients received detailed information regarding advantages and disadvantages of the two types of bladder substitution and urinary diversion. According to patient's preferences, of 102 subjects, 50 (49.0%) underwent ileal conduit urinary diversion, and 52 (51.0%) underwent ileal orthotopic neobladder substitution. All of the participants were naive for ED treatment. Surgery has been carried out in both groups by the same team. The local Medical Ethic Committee approved this study, and all patients gave their informed consent before recruitment into the study.

### Inclusion/Exclusion criteria

Patients were eligible to enter into the study if they had the following inclusion criteria: sexually active and potent preoperatively; married; having bladder confined tumor (clinically  $\leq T3$ ), and had at least one sexual intercourse episode per week. Patients with neurologic or psychiatric disease; previous genitourinary surgery; penile deformity; relationship problems; any endocrinopathy such as diabetes mellitus; previous or concurrent history of chemotherapy or radiotherapy; alcohol or drug abuse; history of myocardial infarction or coronary artery disease; were receiving treatment with known effects on sexual function; and impaired hepatic (serum total bilirubin  $> 2\text{mg}/100$ ) and renal function (serum creatinine  $> 2\text{mg}/100$ ) were excluded from the study.

### Evaluations

All of the participants underwent complete physical examination, medical and sexual history, and laboratory examination including complete blood count, serum electrolytes, serum lipid profile, blood urea nitrogen, creatinine, liver function tests, and sex hormones measurements. The demographic and clinical data, including weight, height, smoking history, occupational status, tumor grade and stage, and types of treatment received were recorded. All patients underwent chest X-ray, computed tomography of the abdomen and pelvis, and whole body

bone scans for tumor staging before treatment. Data regarding comorbid conditions at the time of recruitment were obtained by direct interview and the clinical records.

Sexual function was assessed subjectively by International Index of Erectile Function (IIEF) questionnaire. This questionnaire consists of 15 questions and assesses five sexual domains, including EF (questions 1-5 and 15), orgasmic function (questions 9 and 10), sexual desire (questions 11 and 12), intercourse satisfaction (questions 6 through 8), and overall satisfaction (questions 13 and 14). Of above mentioned domains, only two domains (EF and sexual desire) were evaluated. Patients were followed-up at 1-month interval after surgery, up to twelve months. Follow-up included complete physical examination, medical and sexual history, complete blood count, serum creatinine, blood urea nitrogen, and electrolytes measurements, and blood gas analysis if needed. The questionnaire was administered by a physician 4-weeks before surgery and at 1-month, 6-month, and 12-month postoperative period. Tumors were staged pathologically according to the TNM staging system of the Union Internationale Contre le Cancer (UICC) (14). Tumors grade were determined using the World Health Organization (WHO) classification. Definitions for smoking status were as follow: "ever smoker", who had smoked more than 100 cigarettes in his lifetime, and "former smoker" who had quit smoking for more than 1 year before entry to the study.

Twenty one patients were lost or violated study criteria and finally 81 remained patients were analyzed.

### Statistical analysis

The data were presented as mean  $\pm$  SD. Statistical analysis of continuous variables were carried-out using paired and unpaired, Student t-tests when necessary. Wilcoxon rank sum tests were applied to compare the preoperative and postoperative changes between two study groups. Multivariate linear regression analyses were performed to test the impact of independent variables such as current age, time since diagnosis, smoking history, and stage of tumor at diagnosis on sexual functioning. Differences in individual domain were also examined using

the Mann-Whitney U-test. Statistical significance was set at a P value of  $< 0.05$ . All analyses were performed using SPSS version 17.0 (SPSS, Chicago, IL) for Windows software.

### RESULTS

There were no differences between the groups in the demographic and clinical characteristics (Table-1). Both groups were also comparable according to histopathologic features of bladder cancer. The 41 patients in the ileal loop group had a mean age of  $61.4 \pm 9.4$  years, while the 40 patients in the ileal neobladder group had a mean age of  $61.8 \pm 9.6$  years (Table-1). Postoperatively patients in the both groups demonstrated a significant deterioration in EF domain compared with preoperative values. Erectile function and sexual desire started to improve statistically significantly in ileal neobladder by the 6-month follow up period in comparison to preoperative values. The mean total EF score of the patients at baseline were  $26.74 \pm 1.12$ , and  $26.70 \pm 1.17$ , in ileal conduit and ileal neobladder groups, respectively ( $P = 0.14$ ) (Tables 2, and 3). At 12-month after surgery, these went to  $5.52 \pm 1.24$ , and  $15.60 \pm 1.61$ , in ileal conduit and ileal neobladder groups, respectively ( $P = 0.001$ ), all of the reported P values were adjusted for study confounding factors, including: age, smoking history, tumor stage and grade, time since diagnosis, comorbidity, and body mass index). At follow-up of 12-month, 14 (35.0%) of the ileal neobladder patients were able to achieve vaginal penetration and maintain their erection to completion of intercourse, whereas this was 4 (9.8%) in patients who had underwent ileal conduit ( $P = 0.006$ ). Those 14 and 4 patients had a mean total baseline EF score of  $26.64 \pm 1.43$  and  $26.68 \pm 1.51$ , respectively ( $P = 0.18$ ). These subgroups' mean age of  $60.81 \pm 9.62$ , and  $61.07 \pm 9.37$  in ileal conduit and ileal neobladder groups, did not differ significantly from whole corresponding groups ( $P = 0.42$ ). Among patients in the ileal conduit and ileal neobladder groups, additional 4 (9.8%) and 7 (17.1%) patients were able to get some erection, but were unable to maintain their erection to completion of intercourse ( $P = 0.02$ ).

At the end of 12-month follow-up period, a comparison of two groups showed that 51.2% of

**Table 1 - Distribution of selected demographic and clinical variables among the study groups.**

Variables	Ileal conduit (n = 41)	Ileal neobladder (n = 40)	P value
Age (year)	61.4 ± 9.4	61.8 ± 9.6	0.72
BMI (kg/m <sup>2</sup> )	24.6 ± 4.4	24.4 ± 4.3	0.68
Occupational status No. (%)			
Employed	10 (24.4)	9 (22.5)	0.35
Unemployed	8 (19.5)	9 (22.5)	0.14
Retired	23 (56.1)	22 (55.0)	0.74
Mean ± SD biochemistry			
Blood glucose (mg/dL)	99 ± 12	101 ± 10	0.81
Alanine aminotransferase (IU/L)	29 ± 12	28 ± 14	0.82
Aspartate aminotransferase (IU/L)	28 ± 14	27 ± 12	0.44
Alkaline phosphatase (IU/L)	249 ± 51	247 ± 50	0.62
Total bilirubin (mg/dL)	0.9 ± 0.2	0.8 ± 0.2	0.82
Blood urea nitrogen (mg/dL)	14.2 ± 4.6	14.4 ± 4.4	0.77
Creatinine (mg/dL)	0.9 ± 0.2	0.9 ± 0.1	0.82
Sex hormones			
Testosterone (ng/mL)	6.7 ± 1.5	6.9 ± 1.7	0.65
LH (IU/l)	9.7 ± 2.4	9.9 ± 2.3	0.74
FSH (IU/l)	8.4 ± 2.4	8.8 ± 2.1	0.65
PRL (pmol/L)	372 ± 121	364 ± 123	0.54
Associated comorbidities n (%)			
Arterial hypertension	5 (12.2)	6 (15.0)	0.22
Dyslipidemia	6 (14.6)	5 (12.5)	0.34
Smoking status			
Never	11 (26.8)	12 (30.0)	0.21
Former	10 (24.4)	11 (27.5)	0.27
Current	20 (48.8)	17 (42.5)	0.08
Primary tumor stage			
pT <sub>2</sub>	17 (41.5)	15 (37.5)	0.23
pT <sub>3</sub>	24 (58.5)	25 (62.5)	0.18
Histopathological grading			
G1	6 (14.6)	6 (15.0)	0.83
G2	21 (51.2)	21 (52.5)	0.63
G3	14 (34.2)	13 (32.5)	0.24

**BMI** = body mass index, **LH** = luteinizing hormone, **FSH** = follicle stimulation hormone, **PRL** = prolactin.

**Table 2 - Erectile function and sexual desire domains at baseline and after radical cystoprostatectomy in ileal conduit group.**

Questions*	Baseline	1-month	P value	6-month	P value	12-month	P value**
Question 1: How often were you able to get an erection during sexual activity?	4.44 ± 0.81	0.67 ± 1.20	0.001	0.87 ± 1.31	0.001	1.12 ± 0.92	0.001
Question 2: When you had erection with sexual stimulation, how often were your erections hard enough for penetration?	4.69 ± 0.88	0.71 ± 1.24	0.001	0.77 ± 1.34	0.001	0.56 ± 1.22	0.001
Question 3: When you attempted sexual intercourse, how often you were able to penetrate your partner?	4.45 ± 0.92	0.62 ± 1.25	0.001	0.67 ± 1.27	0.001	0.92 ± 1.12	0.001
Question 4: During sexual intercourse, how often you were able to maintain your erection to completion of intercourse?	4.43 ± 0.84	0.61 ± 1.20	0.001	0.66 ± 1.28	0.001	0.81 ± 1.32	0.001
Question 5: During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	4.35 ± 0.83	0.69 ± 1.22	0.001	0.71 ± 1.26	0.001	1.14 ± 0.91	0.001
Question 15: How do you rate your confidence that you could get and keep an erection?	4.38 ± 0.88	0.58 ± 1.05	0.001	0.62 ± 1.21	0.001	0.97 ± 1.29	0.001
Total erectile function domain score	26.74 ± 1.12	3.88 ± 1.08	0.0001	4.30 ± 1.16	0.0001	5.52 ± 1.24	0.0001
Question 11: How often have you felt sexual desire?	4.21 ± 0.56	1.74 ± 0.65	0.001	2.64 ± 1.24	0.001	2.93 ± 1.21	0.001
Question 12: How would you rate your level of sexual desire?	4.32 ± 0.82	0.89 ± 0.75	0.001	1.74 ± 1.23	0.001	2.21 ± 1.21	0.001
Total sexual desire domain score	8.61 ± 1.17	2.67 ± 1.11	0.0001	4.33 ± 1.19	0.001	5.18 ± 1.31	0.01

\* Questions 1-5 and 15 assess erectile function, score range 1-30, no ED (score of 26-30), mild ED (score of 17-25), moderate ED (score of 11-16) and severe ED (score of 1-10). Questions 11 and 12 assess sexual desire, score range 2-10.

\*\* All P values are vs. baseline

the ileal conduit, and 40% of the ileal neobladder patients rated their sexual desire very low or low ( $P = 0.02$ ). Twenty-four percent of the ileal conduit, and 45.0% of the ileal neobladder patients felt sexual desire high or very high, whether they had sexual attempt or not ( $P = 0.01$ ) (Table-4).

#### Percent changes:

At 12-month postoperative period, among the patients in ileal conduit and ileal neobladder groups, the erectile function total score diminished by 79.4% and 41.2%, respectively ( $P = 0.007$ ) (Figure-1). At 12-month follow-up period, percen-

**Table 3 - Erectile function and sexual desire domains at baseline and after radical cystoprostatectomy in orthotopic ileal neobladder group.**

Questions*	Baseline	1-month	P value	6-month	P value	12-month	P value**
Question 1: How often were you able to get an erection during sexual activity?	4.45 ± 0.82	0.87 ± 1.21	0.001	2.32 ± 1.25	0.01	3.24 ± 1.12	0.02
Question 2: When you had erection with sexual stimulation, how often were your erections hard enough for penetration?	4.62 ± 0.86	0.78 ± 1.22	0.001	1.78 ± 1.32	0.006	2.67 ± 1.21	0.02
Question 3: When you attempted sexual intercourse, how often you were able to penetrate your partner?	4.47 ± 0.87	0.72 ± 1.21	0.001	2.25 ± 1.21	0.01	2.94 ± 1.14	0.03
Question 4: During sexual intercourse, how often you were able to maintain your erection to completion of intercourse?	4.42 ± 0.82	0.66 ± 1.20	0.001	2.61 ± 1.27	0.01	2.57 ± 1.27	0.03
Question 5: During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	4.39 ± 0.81	0.66 ± 1.20	0.001	1.78 ± 1.21	0.006	2.14 ± 1.32	0.02
Question 15: How do you rate your confidence that you could get and keep an erection?	4.34 ± 0.86	0.62 ± 1.04	0.001	2.22 ± 1.15	0.01	1.98 ± 1.21	0.01
Total erectile function domain score	26.70 ± 1.17	4.31 ± 1.04	0.0001	12.94 ± 1.42	0.001	15.60 ± 1.61	0.001
Question 11: How often have you felt sexual desire?	4.24 ± 0.55	1.81 ± 0.61	0.001	2.89 ± 1.24	0.01	3.12 ± 1.14	0.04
Question 12: How would you rate your level of sexual desire?	4.36 ± 0.77	0.88 ± 0.78	0.001	2.14 ± 1.23	0.01	2.68 ± 1.27	0.02
Total sexual desire domain score	8.64 ± 1.12	2.70 ± 1.14	0.0001	5.10 ± 1.15	0.01	5.77 ± 1.32	0.01

\* Questions 1-5 and 15 assess erectile function, score range 1-30, no ED (score of 26-30), mild ED (score of 17-25), moderate ED (score of 11-16) and severe ED (score of 1-10). Questions 11 and 12 assess sexual desire, score range 2-10.

\*\* All P values are vs. baseline.

tage changes from baseline in question 2 (erection firmness), were -66.0%, and -43.5%, in ileal conduit and ileal neobladder groups, respectively (P = 0.005). These were -74.4% and 52.3% for question 5 (maintenance ability), respectively (P = 0.01) (Figure-1). At the end of follow-up period, again patients with ileal conduit had 41.9%, and patients with ileal

neobladder had highest 33.7% decrease in sexual desire domain of IIEF (P = 0.02) (Figure-2).

#### Complications:

There were no operative mortalities. There was no death in 12-month follow-up in both groups. Early complications were seen in 5 patients

**Table 4 - Responses to erectile function and sexual desire domains questions from IIEF questionnaire after radical cystoprostatectomy at 12-month postoperatively.**

Response	Question 1		Question 2		Question 3		Question 4	
	IC	INB	IC	INB	IC	INB	IC	INB
Did not attempt intercourse	0	0	0	0	0	0	0	0
Never/occasionally	27	20	30	18	29	18	31	17
Less than half the time	4	3	3	3	3	3	4	4
Sometimes/half the time	4	4	3	3	3	3	3	3
More than half the time	2	2	1	2	2	2	3	2
Almost always	4	12	4	14	4	14	3	14
P value	0.008		0.006		0.006		0.005	

Response	Question 5		Question 15	Question 11		Question 12			
	IC	INB		IC	INB	IC	INB		
Did not attempt intercourse	0	0	Very low	9	9	11	7	9	6
Extremely difficult	22	14	Low	14	8	15	10	12	10
Very difficult	6	6	Moderate	5	2	7	8	9	6
Difficult	6	4	High	4	10	6	6	7	9
Slightly difficult	2	4	Very high	9	11	2	9	3	9
Not difficult	5	12	P value	0.003		0.006		0.005	
P value	0.005								

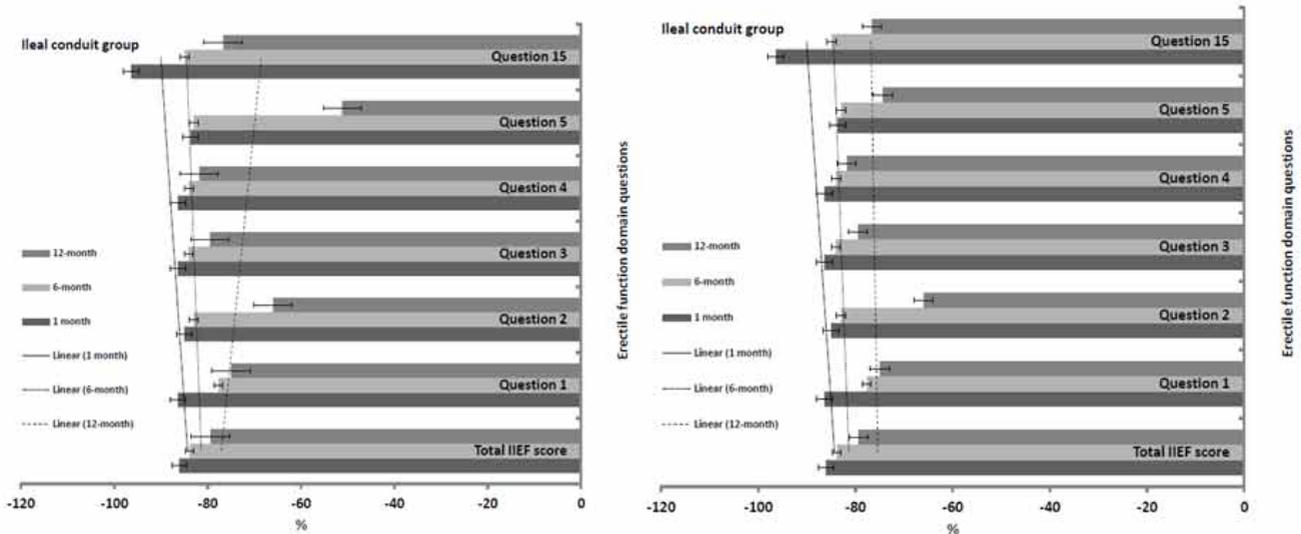
IIEF = International Index of Erectile Function, IC = Ileal conduit, INB = ileal neobladder.

(12.2%) in the Ileal conduit group (two prolonged ileus, one wound infection, one anastomotic stricture and one diarrhea) and 6 patients (15.0%) in the ileal neobladder group (two prolonged ileus, two wound infection, one anastomotic stricture, and one urolithiasis) ( $P = 0.87$ ). Ureteral anastomotic stricture was corrected by re-operation.

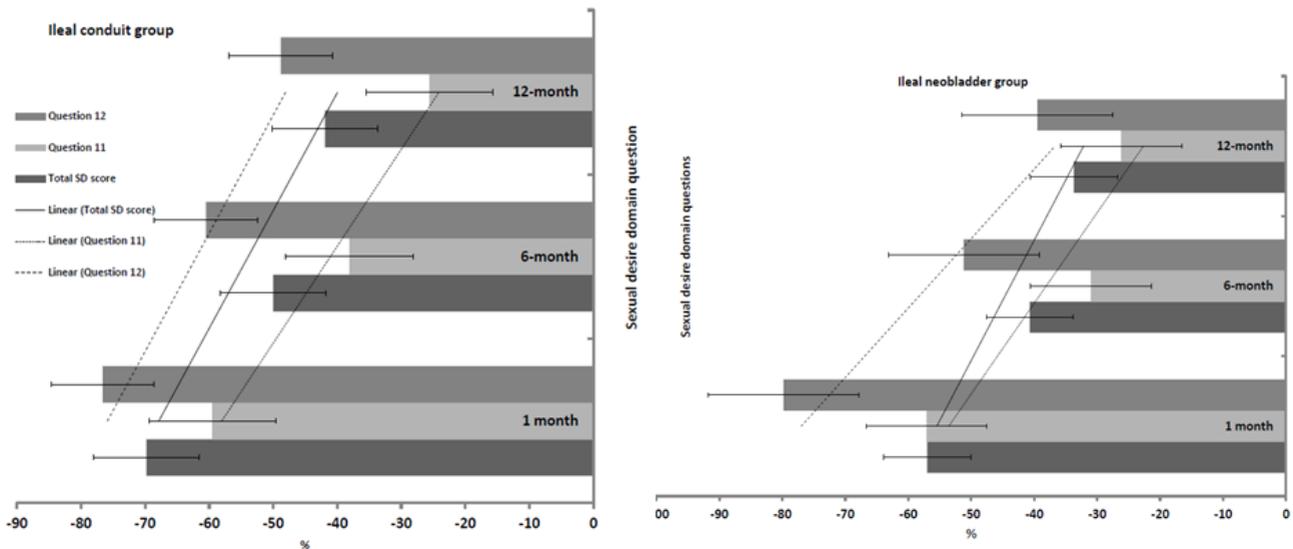
## DISCUSSION

This study demonstrated that patients with orthotopic ileal neobladder substitutes had more favorable erectile function and better sexual desire than patients with ileal conduit. Ileal urinary diversion after RCP is the safest for cancer control,

**Figure 1 - Percent changes from baseline in erectile function domain total score and questions during follow-up period. Bars represent error bars with standard error.**



**Figure 2 - Percent changes from baseline in sexual desire domain total score and questions during follow-up period. Bars represent error bars with standard error.**



have the lowest complication rates, and afford the easiest adjustment for patients' lifestyle (13). Complete and severe erectile dysfunction after radical cystectomy is a well known complication. One measure to reduce this devastating complication is performing nerve sparing surgery. Nerve sparing surgery is criticized because of the com-

promising cancer control (15) and concerns about the rate of recoverability of erectile function after nerve sparing surgery. Schoenberg et al. reported that recovery of erectile function following nerve sparing surgery is 20% in patients older than 60 years (16). Before recruitment in present study, the advantages and disadvantages of nerve

sparing surgery were discussed thoroughly with the patients, and all of them choose to proceed with non-nerve sparing surgery. The results of this study have important implication. During the past decade, RCP has focused primarily on cure, recurrence, and continence, and an important complication after this procedure (erectile dysfunction) has not been addressed adequately. Our results demonstrate that, psychological factor is an important aspect of sexual function after RCP. Hobisch et al. compared patients with an ileal conduit and those with orthotopic neobladders using European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Version 3.0 (EORTC QLQ C-30) (17). In their study the orthotopic neobladders scored significantly better than the ileal conduit in all domains. However, there are other studies in which the authors couldn't detect any statistically significant difference in quality of life between incontinent and continent lower urinary tract reconstruction (18-20). The potential influence of sociocultural settings on the sexual functioning after RCP and lower urinary tract reconstruction must be appreciated. Over the last decade, some efforts have been made to assess quality of life after RCP and lower urinary tract reconstruction; however, no study has compared the erectile function in patients with an ileal conduit, and orthotopic ileal neobladder. Patients with an ileal conduit have urinary leakage from the stoma and as a result may smell urine odor and disturb at office, sleeping, bathing and traveling. Having a stoma may make the ileal conduit patients reluctant to engage in sexual activity. We also speculate that lower sexual desire was based on having a stoma. The reported rate of erectile function after conventional RCP ranged between 14% and 80% (2-4). This vast difference could be explained by surgeon's skill, population studied, outcome measure instruments, as well as patients expectation and sociocultural norms and issues. One should make every effort to increase the recoverability of erectile function after RCP, without compromising the cancer surgery results. In the present study, after controlling for confounding factors, such as age and comorbidity, type of urinary diversion (ileal conduit vs. orthotopic ileal neobla-

dder) independently affects EF and sexual desire domains scores. The impact on EF and sexual desire domains was small yet statistically significant and might be more obvious with larger sample sizes. Our results demonstrate that, postoperatively, after significant deterioration of erectile function in both groups, there was a progressive improvement in EF and sexual desire scores in a small proportion of patients with orthotopic ileal neobladder, started to differ significantly between two groups by the end of 6-month follow-up periods. An explanation could be that with time patients undergo psychological adaptation and thus any negative feelings about their body image may affect their sexual function. We speculated that, in addition to stoma related problems, patients with ileal conduit have negative feelings regarding the altered body image generated by the treatment. Apparently, patients with orthotopic ileal neobladders have increased cosmetic results and the potential for voiding via natural conduit with no abdominal stoma and no need for external appliance. A small proportion of patients in both groups (9.8% in ileal conduit and 17.1% in ileal neobladder group) were able to get some erection, but were unable to maintain their erection to completion of intercourse. This subset of patients might be responders to 5-phosphodiesterase inhibitor administration.

The current study was limited by its small number of patients. In addition, patients were evaluated subjectively. Because all of the patients underwent non-nerve sparing RCP, therefore we did not attempt to evaluate penile neurovascular integrity objectively.

## CONCLUSIONS

There were significant differences in EF and sexual desire domains between ileal conduit and orthotopic ileal neobladder diversion groups. Therefore, orthotopic ileal neobladder it is the best option especially in younger patients requiring RCP.

## CONFLICT OF INTEREST

None declared.

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