African Journal of Urology (2013) **19**, 89–93

Pan African Urological Surgeons' Association

African Journal of Urology

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Long term complications after radical cystoprostatectomy with orthotopic diversion in male patients: Preliminary experience

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Received 22 November 2012; received in revised form 8 February 2013; accepted 22 February 2013

KEYWORDS
Long term;
Complications;
Follow up;
Radical;
Cystoprostatectomy;
Urinary diversion

Abstract
Introduction: Radical cystectomy is the standard treatment for patients with invasive bladder cancer and for those with superficial bladder cancer who did not respond to conservative TUR and intravesical therapy. Many diversions are available after radical cystectomy; the most attractive for the patients is orthotopic diversion due to better quality of life associated with this diversion.
Objective: To evaluate the long-term outcomes beyond 1 year, both functional and oncological, in male patients treated with radical cystectomy and orthotopic diversion for invasive bladder cancer.
Patients and methods: This is a retrospective study done at Cairo university hospitals. A total of 44 male patients underwent radical cystectomy and orthotopic diversion (W-pouch) for invasive bladder cancer with minimum follow up 1 year. Assessment included; neobladder function, renal pattern and function, ureteroenteric anastomotic stricture or reflux, survival, recurrence, erectile function, urolithiasis, and urinary tract infection.
The tools used to assess the complications during each visit included; history including voiding diary and IIEF questionnaire, examination including PR, laboratory investigations including urine analysis and kidney function tests, pH (acidosis) and bicarbonates and radiological investigation including ultrasound, chest X-ray, CT abdomen and pelvis.

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Peer review under responsibility of Pan African Urological Surgeons' Association.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.afju.2013.02.008

Results: The mean follow up was 88 months (range 12–138). Stones developed post-operatively in four patients (two of them were pouch stones and the other two were renal stones), incision hernia developed in two patients (4.5%), uretero enteric anastomotic stricture in two patients (4.5%), recurrent UTI was recorded in 10 cases (23%), uremia and dialysis in 9.2% of cases, metastasis was recorded as follows: local 2%, distant 11.5% and both 4.5% and the mortality rate was 19% (over all survival was 81%).
Nocturnal incontinence 29.5% (13 patients), stress incontinence 9.5% (4 patients), urge incontinence 9.5% (4 patients), total incontinence 4.5% (23 patients); while the remaining 21 patients (47.5%) were continent day and night.
Erectile dysfunction developed post-operatively in 35 cases (80.5%).
Conclusion: Long term follow-up for patients with radical cystectomy and orthotopic diversion is associated with high complication rate. Long term follow up for those patients is needed to verify the causes of complications and how to prevent them.

Introduction

Urinary bladder cancer is the second most common malignancy of all genitourinary tumors after prostate cancer and is nearly three times more common in men than in women [1]. In Egypt, carcinoma of the bladder is the main oncologic problem. At the National Cancer Institute (NCI), Cairo, urinary bladder cancer constitutes 30.3% of all cancers, 40.6% of male cancers, and 14.3% of female cancers [2].

According to the International Agency for Research on Cancer (IARC) statistical study, Egypt ranked first among Northern African and Arabian African countries in urinary bladder cancer incidence and mortality rates in both males and females [3].

This study was done to evaluate long-term outcomes, both functional and oncological, in male patients treated with radical cystectomy and orthotopic diversion for invasive bladder cancer at Cairo university hospitals.

Patients and methods

This retrospective study was conducted in Kasr EL-Aini hospital and student hospital and included 44 male patients in the period from May 2000 to May 2001, who underwent radical cystectomy with ileal neobladder diversion (W-pouch) (Fig. 1) for bladder malignancy. Follow up of those patients continued to May 2012.

Data were collected through follow-up visits every 3 months in the first year, and then for every 6 months from the second year with a mean follow up of 88 months (range 12–138 months).

Every patient was evaluated by the following.

History included: age and risk factors (bilharziasis, smoking, diabetes mellitus, hypertension, ischemic heart disease).

Operative details, post-operative pathological analysis (staging and pathological subtypes), and post-operative adjuvant treatment (radiotherapy or chemotherapy) were recorded.

History of lower urinary tract symptoms, hematuria, fever, or loin pain were also reported.

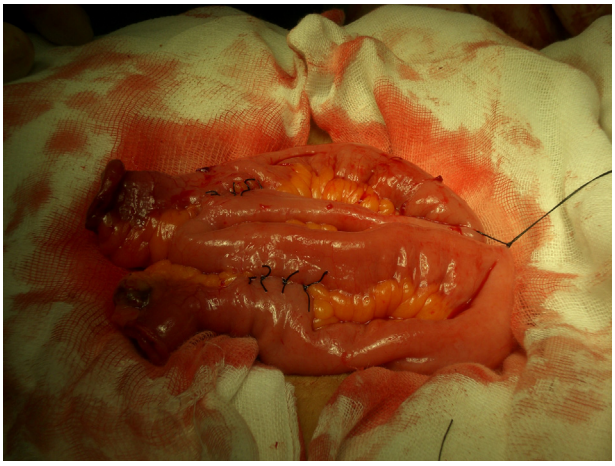

Figure 1 Ileal neobladder diversion (W-pouch).

Physical examination included: general examination for pallor and cachexia, abdominal examination for masses, nodules, scars of previous operations, and per rectal (PR) examination for tenderness, masses, and nodules.

Imaging study included: abdomen and pelvis U/S, CT abdomen and pelvis, CT chest and Bone scan when needed.

Laboratory study included: serum creatinine, complete blood picture, serum sodium, serum potassium, and urine analysis, culture and sensitivity. pH (acidosis) and bicarbonate was done when indicated.

Diurnal and nocturnal voiding rates were retrieved from the voiding diary. The number of nocturnal awakenings and the relation to nocturnal continence, necessity of use of protective pads (by day and/or night) and the use of any medications that may help improving continence, were all clearly defined.

Diurnal continence was defined as complete dryness without stress leakage or use of protective pads.

Nocturnal continence was defined as complete dryness without the need for protective pads, multiple awakenings (more than twice) or drugs.

Table 1 Staging and pathological subtypes in 44 cases.

	Number	%
Staging		
T1	0	0
T2a	4	9.0
T2b	36	82.2
T3a	3	6.5
T3b	1	2.3
T4	0	0
N1	3	6.5
N2	3	6.5
Pathological subtypes		
TCC	37	84.5
SqCC	5	11.0
Adenocarcinoma	2	4.5

The International Index of Erectile Function [IIEF] questionnaire was used to assess erectile function.

Statistical analysis

Data were statistically described in terms of range, mean ± standard deviation (SD), median, frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Mann–Whitney *U* test for independent samples. For comparing categorical data, Chi square test was performed. Exact test was used instead when the expected frequency is less than 5. *P* values less than 0.05 was considered statistically significant.

Results

Demographic data

This study included 44 male patients whom underwent radical cystectomy (RC) operation and orthotopic diversion for invasive bladder cancer.

The mean age was 63.5 years (range 35–78 years).

Six patients (13.8%) were pre-operatively diabetics (DM), 10 patients (23.0%) had hypertension (HTN), 3 patients (6.5%) had ischemic heart disease (IHD), 30 patients (69%) were smokers and 15 patients (34.5%) had history of bilharziasis.

Postoperative pathological analysis revealed; transitional cell carcinoma (TCC) in 37 patients (85%), squamous cell carcinoma (SqCC) in five patients (11.0%), while adenocarcinoma was reported in two patients (4.05%). Table 1 shows the postoperative pathological sub types and staging.

Forty patients (91%) did not receive post operative chemo- or radiotherapy, while two patients received post-operative radiotherapy (due to enlarged pelvic lymph nodes in their follow up imaging in one case and due to advanced post-operative pathological stage (T3b) in the other case), one patient received chemotherapy (due to enlarged para-aortic lymph nodes) and one patients received chemo and radiotherapy (due to pelvic metastasis and enlarged para-aortic and supraclavicular lymph nodes), no one received pre-operative chemo- or radiotherapy.

Table 2 The main long term complications.

Complication	Number	%
Stones	4	9.0%
Pouch stones	2	4.5%
Renal stones	2	4.5%
Recurrent urinary tract infection	10	23.0%
Uretero enteric stricture	2	4.5%
Renal function deterioration	4	9.0%
Bilateral hydronephrosis	2	4.5%
Bilateral hydronephrosis and hydronephrosis	2	4.5%
Bilateral hydronephrosis	3	6.5%
Bilateral nephropathy	5	11.5%
Erectile dysfunction	35	80.5%
Recurrence	8	18.4%
Local	1	2.3%
Distant	5	11.5%
Both	2	4.6%
Incontinence		
Nocturnal incontinence	13	29.5%
Total incontinence	2	4.6%
Stress incontinence	4	9.5%
Urge incontinence	4	9.5%

Six patients (13.8%) had enlarged pelvic lymph nodes (LNs), five patients (11.5%) had enlarged para-aortic LNs, and one patient (1.5%) had enlarged supraclavicular LN detected during their follow up imaging beyond 1 year postoperatively.

The reported complications

Table 2 shows the long term complications.

Erectile dysfunction (ED): Thirty five patients (80.5%) had ED (IIEF score is less than 25); they were treated with sildinafil or intracorporeal prostaglandins injection, 2 patients (4.6%) were potent (score more than 25) while only 7 patients (15.0%) were impotent pre-operatively.

Urinary continence: Twenty one patients (47.7%) were continent day and night, 13 patients (29.5%) had nocturnal incontinence and complete diurnal continence, four patients (9.5%) had stress incontinence, four patients (9.5%) had urge incontinence and two patient (4.6%) had total incontinence; the last two patients were treated with male sling.

Urolithiasis: four patients (4.5%) developed postoperative stones: two patients had pouch stones treated by cystoscopic crushing and the other two patients developed renal stone treated by PCNL.

Uretero-intestinal anastomotic stricture: it was reported in two cases (4.5%): they were treated by percutaneous nephrostomy and then antegrade ureteric stenting in one case and percutaneous nephrostomy, and then cystoscopic dilatation of the ureters and ureteric stenting in the other case.

Recurrent urinary tract infection (UTI): it was reported in 10 patients (23%), they were treated by oral antibiotics and/or intravenous fluids and antibiotics according to the severity of infection.

Postoperative follow up imaging (abdominal and pelvic ultrasound and or CT abdomen and pelvis) revealed that three patients (6.5%)

Table 3 The mortality rate and causes of mortality.

Complication	Number	%
Mortality rate	8	18.4%
Causes of mortality		
Distant metastasis	3	6.5%
Distant metastasis and renal failure	3	6.5%
Heart failure	1	2.3%
Unknown	1	2.3%

developed bilateral hydronephrosis (HN), five patients (11.5%) had bilateral nephropathy.

Uremia and dialysis: four patients (9.5%) developed uremia and on regular dialysis, two patients due to bilateral nephropathy, and two patients due to bilateral hydronephrosis and nephropathy.

Metastasis: five patients developed distant metastasis, one patient developed local metastasis and one patient with developed both local and distant metastasis.

Mortality and causes of death (Table 3): eight patients (19%) died, three patients (6.8%) died from distant metastasis, and three patients (6.8%) died from renal failure and distant metastasis, one patients died from heart failure and one patient died due to unknown cause.

Thirty six cases still alive at mean follow up of 80 months (range 12–138 months).

Discussion

Radical cystectomy (RC) with pelvic lymph node dissection provides the best cancer-specific survival for muscle invasive urothelial cancer [4,5] and is the standard treatment, with 10-year recurrence-free survival rates of 50–59% and overall survival rates of around 45% [4,6]. RC with urinary diversion (UD) is a procedure in which reduction of morbidity, rapid postoperative rehabilitation, limited length of hospital stay, and cost containment are difficult to achieve [7]. The primary goals in selection of a urinary diversion are to provide the patient with diversion that results in the best local cancer control, the lowest potential for complications both short and long, and the best quality of life while still allowing the timely completion of chemotherapy and therapeutic goals [8]. Single institution experiences worldwide have reported favorable short-term oncologic outcomes and the controversy regarding long-term oncologic results still exists [9,10].

In our study, 35 patients (80.5%) developed ED postoperatively (in addition to 15% were impotent preoperatively), 80% of them were smokers, 15% were diabetics, 20% had hypertension, 10% had ischemic heart disease and their mean age was 68 year, while only 4.5% were potent, in addition, all of those patients were not known to have nerve sparing cystectomy. The multiple risk factors, the age, the way of ED assessment and the absence of nerve sparing techniques in our patients may explain the high rate of ED in our study. In other studies, nerve-sparing cystectomy has better results, where 78.8% were potent [11]. In another study 86% developed impotence postoperatively, while only 14% of patients were potent postoperatively (7 of 49 patients), of those 7 potent patients, 6 patients had undergone nerve-sparing cystectomy [12].

In our study, nocturnal incontinence after non-nerve sparing RC was 29.5%, while in El-Bahnasawy et al. study [13] nocturnal incontinence after non-nerve sparing RC was 36.7%. Some of the studies have high results in urinary continence like that of Jian and co-workers [14] in which nocturnal continence after laparoscopic radical cystectomy (LRC) is 82.5%, LRC with different urinary diversion methods has been demonstrated to be feasible, safe, and capable of providing many intraoperative and postoperative advantages, However, the oncologic safety of this procedure is still being evaluated, and report of patients with >5-year follow-up are unavailable [14].

In our study, 9% developed urinary stones after RC, while in a study done by Lawrentschuk et al., urinary stones after RC incidence was 3.9–9% [15], another study done by Thorsten son et al., showed an incidence of 2.7% (4 patients of 148) developed urinary stones after more than 90 days of RC [16]. While in the study of El-Sayed, urinary stones incidence was 10.5% this may be due to longer follow up period (mean follow up period was 50 months while ours was 88 months) [17].

Incisional hernia was recorded in two cases (4.5%), and in other studies incisional hernia was 6.7% and 5.2% [16,18]. In our study recurrent UTI was recorded in 23% of cases, and in other studies recurrent UTI was recorded by Thorsten son et al. [16] in 21.6%, by Jakko et al. [18] in 32.8% and by El-Sayed [17] in 23.7%.

Deterioration of renal function was recorded in four cases (9.2%) in our study, which is comparable to other investigators as it is (10.8%, 12%, 23.7%, and 0.3–27% [16–20]).

In our study, there was local recurrence in one case 1.5%, distant metastasis in five cases (11.5%) and both local and distant in two cases 4.6%, while in a study by Jian et al. [14] there was local recurrence in 9 patients (5.3%), distant metastasis in 23 patients (13.5%) and both in two patients (1.2%).

In our study, 8 patients (19%) had died from various causes; three patients (6.5%) died from distant metastasis, three patients (6.5%) died from renal failure and distant metastasis, one patient died from heart failure and one patient died due to unknown cause, while in the study of Jian et al. [14] there were 28 of 171 patients (16.4%) had died from various causes, 20 from metastasis and 8 from causes unrelated to the tumor (two from upper gastrointestinal bleeding, two from myocardial infarction, two from pneumonia, one from stroke and one from a car accident).

The intervention rate in our patients was high (8 cases 18.4%); and included interventions for, two cases of pouch stones, two cases of renal stones, two cases of ureteroenteric stricture, and two cases of total incontinence. At the last follow up (mean 88 months), every patient had experienced one or more of the late complications.

Conclusions

Long term follow-up for patients with radical cystectomy and orthotopic diversion is associated with high complication rate. Long term follow up for those patients is needed to verify the causes of complications and how to prevent them.

Conflict of interest

No conflict of interest.

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