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ORIGINAL ARTICLE

10–YEARS AFTER A SIMPLE TECHNIQUE OF NERVE SPARING RADICAL CYSTECTOMY FOR T_2 BILHARZIAL BLADDER CANCER

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Abstract

Aim: This study was done to evaluate the results of the surgical technique described herein regarding the post-operative functional results as well as achievement of loco-regional control of the disease and to assess the long term outcomes.

Patients and Methods: Between January 1999 and December 2003, 40 selected, consecutive male patients (median age: 50 years, range; 30-67) with stage T_2 biharzial bladder cancer were treated by the technique described herein of nerve sparing radical cystectomy and urinary diversion at Cairo National Cancer Institute hospital and in the Pyramid hospital at Cairo. The patients were followed up for 10 years after surgery to detect any local or distant recurrence of the disease and to evaluate their potency.

Results: At 10-Year follow-up period (median follow-up period was 138 months, range:109-168): 34 (85%) patients were alive and free of cancer, from whom 26 (65%) patients were potent and 8 (20%) patients have lost their erectile function. 3 (7.5%) patients died from local recurrence of the disease at 38, 53, 75 months after surgery, while 3 (7.5%) patients died from causes other than cancer at 113, 115 and 130 months after surgery.

Conclusion: To conclude that the aforementioned described modifications of the technique of standard radical cystectomy, which is simple, reduced the morbidity of radical cystectomy without altering its therapeutic efficacy.

Keywords: Nervi erigents sparing, Schistosomiasis, bladder cancer, surgery.

INTRODUCTION

Urinary blabber cancer ranks the ninth in worldwide cancer incidenece.(1)

Bladder carcinoma arising in association with bilharzial cystitis presents distinct clinicopathologic features quite different from the reported in western counties.(2,3) It affects patients at a much younger age (mean: 46 years).(4) The tumor is usually localized to the bladder with a limited tendency to lymphatic and blood spread.(2-4) Three decades ago, bladder carcinoma was the foremost national oncologic problem in Egypt, but in recent years a significant decline in its frequency was

observed becoming second after breast and contributing only 11% of all cancers.[5]

The quality of life is an important issue in the treatment of young males with bilharzial bladder cancer. The hope is to establish a simplified technique of nerve sparing radical cystectomy without compromising the principles of oncologic surgery, thus affording loco-regional control of the disease with potency preservation. Since Walsh and his colleagues[6-9] had defined the retropubic anatomy and introduced the concept of intra-operative cavernous nerve area identification, many surgeons attempted nerve sparing radical cystectomy. Different techniques of nerve sparing radical cystectomy were described and resulted in favourable outcomes. In 1996, Schoenberg and his colleagues[10] published their 10-Year follow up results of 101 male patients with organ confined bladder cancer who were treated in the period from 1982 to 1989 utilizing Walsh procedure of nerve sparing cystoprostatectomy. In 2001, Horenblas and his colleagues[11] published their work of nerve sparing radical cystectomy for ten men with early bladder cancer who were operated in the period from 1995 to 1998 with preservation of the neurovascular bundles, vasa deferentia, prostate and seminal vesicles. In 2002, Vallancien and his colleagues[12] published their work of nerve and prostate sparing radical cystectomy for 100 male patients with organ confined bladder cancer who were operated since 1992. In 2001, Colombo and his colleagues[13] published their work of nerve sparing radical cystectomy for eight men with superficial bladder cancer, their procedure consisted of transurethral resection of the prostate, pelvic iliac node dissection and extraperitoneal cystectomy performed while preserving the neurovascular bundles, the vas deferens and the seminal vesicles. In 2004, Colombo and his colleagues[14] published their work on the outcomes of their technique on 27 men with T_1 and T_2 bladder cancer. In 2004, Muto and his colleagues[15] published their work of seminal sparing cystectomy for 63 male patients (T_1:58,T_2:5) who were operated in the period from 1990 to 2002, in their technique, the posterior bladder dissection is anterior to the seminal vesicle plane to preserve the vasa deferens, seminal vesicles, prostatic capsule and neurovascular bundles. In 2005, Salem[16] described preservation of ejaculatory and erectile function in seven men with early bladder cancer located in anterior or lateral bladder wall. In 2007, Salem[17] published the results of four patients who were treated in the period from 2002 to 2004 by his new technique of nerve sparing radical cystectomy with preservation of the seminal vesicles and vas deferens. Some of these surgical techniques are easy and simple, but most of these techniques are tedious and need prolonged training in order to master the sophisticated surgical steps. But in fact, the simplified surgical technique of nerve sparing radical cystecotomy described in this present work is an easy simple technique and can be performed properly by the average surgeon. The steps of this technique are very similar to the technique of standard radical cystectomy described by Skinner and Leiskovsky[18] but with certain simple and clear easy modifications.

This present work of simplified technique of nerve sparing radical cystectomy is mainly based on the principle of do not disrupt or interrupt the pathway of the neural fibres of the nervi erigents that will conform the cavernous nerves. Throughout the steps of this procedure, the integrity of these nerves was protected without compromising the principles of oncologic surgery. It is mandatory to know and realize the exact anatomy and the precise topographic anatomy of the nervi erigents which became well established.

This study was done to evaluate the results of the surgical technique described herein regarding the post-operative functional results as well as achievement of loco-regional control of the disease and to assess the long term outcomes. From an oncological point of view, long–term follow up is of paramount importance to confirm whether this surgical procedure can be proposed as a valid choice of treatment for young, fully potent and socially active male patients with T_2 bilharzial bladder cancer.

MATERIAL AND METHODS

Between January 1999 and December 2003, forty consecutive male patients were selected according to the criteria of patient selection (stage T_2 bilharzial bladder cancer with good erectile function); their median age was 50 years (range: 30-67). The patients were treated by this technique of nerve sparing radical cystectomy and urinary diversion at Cairo National Cancer Institute hospital and in the Pyramid hospital at Cairo. The patients were followed up for 10 years after surgery to detect any local or distant recurrence of the disease and to evaluate their potency.

Criteria of patient selection:

1. All patients were considered to have stage T_2 bilharzial bladder cancer on the basis of their clinical and radiological staging. According to the American Joint Committee on Cancer 2002 TNM Bladder Cancer Staging:[19] T_2 means that tumor is confind to the muscle wall of the bladder. T_3 means that tumor invades perivesical tissue ($_pT_{3a}$: Microscopically, $_pT_{3b}$: Macroscopically).

2. The lower edge of the tumor should be 3cm or more from the bladder neck as evidenced by cystoscopy. For these patients complete prostatic removal was not necessarily mandated by the tumor.

3. Preliminary diagnosis of schistosomiasis was based on past history or cystoscopic biopsy. Confirmation of this diagnosis was only valid when there was a histologic evidence of bilharziasis in the post–

surgical specimen.

4. Selected patients were sexually active males in whom erectile function was an important quality-of-life issue before surgery.

Pre–operative evaluation:

1- The tumor should be confined to the muscle wall of the bladder as evidenced by pelvic CT.

2- Routine investigations for fitness for a radical cystectomy: HB% should be above 10gm%, serum albumin above 3gm%, prothrombin concentration above 85%, blood urea should be less than 40 mg %, serum creatinine less than 1.5 mg% and the x-ray chest was normal to include the patient in the study.

3- Pre–operative Doppler study to the penis should be normal.

Operative technique: After abdominal exploration for operability, all the principle steps of standard radical cystectomy were performed in the same manner as previously described by Skinner and Leiskovsky[18] but with some modifications to preserve potency, the modifications were based on the principle of do not disrupt or interrupt the pathway of the neural fibres of the nervi erigents that will innervate the corpora cavernosa. Because the studied patients were bilharzial, the extent of lymph node dissection was followed according to the technique previously described by EL-Sebai.[3] The limits of lymph node dissection included: the mid common iliac vessels proximally, the genitofemoral nerve laterally (including the nodes related to the origin of inferior epigastric and deep circumflex iliac vessels), the nodes situated behind Pouparts ligament distally (including the lymph node of Cloquet) and the obturator nodes medially .The obliterated umbilical and superior vesical arteries were identified and transected at their origin .The inferior vesical artery was protected and only its branches that will enter the bladder were ligated very close to the bladder, and the same for the branches which supply the seminal vesicles. Its maintained branch (the prostatic artery) is scaffolded by the neural fibres of the nervi erigents and should be protected during the steps of posterior dissection of the bladder.

During posterior dissection, no dissection was done deeper than the anterior wall of the rectum in order to protect the autonomic pelvic plexus and posterior dissection was continued down to 1.5 cm beyond the base of the prostate. The prostate was divided in a slanting way in order to conserve a wide area of its capsule and the overlying visceral endopelvic fascia, in which the neurovascular bundle is imbedded. The distal two thirds and the apex of the prostate were preserved without mobilization. The endopelvic fascia which cover the prostatic capsule was preserved.

Haemostasis was achieved by transfixing the bleeding points at the cut edge of the prostatic capsule. Haemostasis was completed without using diathermy at the sites of the proposed pathway of the neural fibres. When further haemostasis of the prostatic venous plexus was needed which may endanger the cavernous nerves, the superficial branch of deep dorsal vein of penis was ligated in continuity. In this situation division of puboprostatic ligaments was done and a thread of 2/0 vicryl is passed infront of the urethra to ligate the vein in continuity (at this level the cavernous nerves lie posterolateral to the urethra, and this vein lies outside the endopelvic fascia). This surgical step was derived from the technique previously described by Reiner and Walsh.[20]

When orthotopic neo-bladder was considered, the anastomosis was done in a way that the needle and suture material will not injure the spared neural fibres. The needle was passed from inside the lumen of the prostatic urethra and pass deeply inside the prostatic tissue and then come out inside the prostatic capsule just biting the rim of edge of capsule.

Urinary diversion was done in the form of orthotopic ileocecal neo–bladder utilizing the technique previously described by Khafagy and his colleagues.[21] The abdomen was closed and drained using two wide bore tubes attached to closed suction drainage. The average operating time was 2.5-4 hours and the average blood loss was 700ml.

Assessment of potency:

1- Assessment of potency began one month after hospital discharge by doing a postoperative Doppler study of the penis for all patients. Potency was reported subjectively from patients. For all patients we relayed upon their telling about themselves. The sexual activity before surgery was considered and compared to the present activity after surgery.

2- The Rigiscan system was not available for nocturnal penile erection measurement. Instead, the stamp ring test was used as the available night tumescence test.

The follow–up schedule: The follow–up schedule was clinical examination (including bimanual rectal examination), laboratory and radiological investigations (including pelvic CT). The patients were followed up every 3 months for the first 2 years and then every 4 months till the end of 5th year. Then every year till the end of the 10th year .In every follow up visit, beside the routine work up to detect any local or distant metastasis, fine history of the details of the sexual act was conducted.

RESULTS

Post–operative results:

I. **Surgery:**

- There was no intraoperative complications.
- Convalescence was uneventful in 34 patients.
- Four patients developed a minor urinary leakage (less than 300/ml per day) which improved conservatively.
- Skin wound sepsis occurred in 2 patients.

II. **Histopathologic examination:** Histopathologic examination of the forty post–surgical specimens confirmed that the stage of the disease was pT_2 in all patients. All specimens showed a negative prostatic urethral surgical margin. All specimens were positive for bilharzial eggs. Different tumor types, histological grades and pelvic nodal status of 40 patients are shown in (Table 1).

III. **Potency preservation:** All the Doppler studies performed one month after hospital discharge were normal for all patients .Sixteen (40%) out of 40 patients reported early normal erections to occur in the period from 1 to 6 weeks after hospital discharge and they reported satisfactory sexual activity, from whom 2 patients reported erections to start in days 9,10 after surgery with the indwelling catheter in place. Thirteen out of 40 patients reported weak (unsatisfactory) erections to occur in the period from 1 to 6 weeks after hospital discharge while another 4 patients reported weak erections to start after more than 6 weeks from hospital discharge. (Table 2) shows the time of start of erections and the quality of erections (normal or weak) for 33 patients. The seventeen patients (42.5%) with weak unsatisfactory erections were helped by Sildenafil tablets. With the help of Sildenafil tablets, these 17 patients gained normal erections and satisfactory sexual activity. Seven (17.5%) out of 40 patients reported no erection to occur up to 12 months after surgery although their postoperative Doppler studies were normal. These 7 patients did not gain a help by using Sildenafil tablets. It is noteworthy to mention that Sildenafil tablets do not affect the symptom of patients with injured nervi erigents and intact nerves are required for Sildenafil to work. These 7 patients were negative for the night tumescence test (stamp ring test) and hence psychogenic impotence was excluded. They were considered to be impotent due to lack of sparing of the neural fibres that supply the corpora cavernosa during the operative procedure.

Table 1. Different tumor characteristics of 40 patients.

Characteristics	No. of patients	Percentage
Pathological types:		
Squamous cell carcinoma	26	65
Transitional cell carcinoma	14	35
Histological grade:		
G1	17	42.5
G2	19	47.5
G3	4	10
Pelvic nodal status:		
+ ve LNs	6	15
- ve LNs	34	85

Table 2. Time of start and quality of erections (normal or weak).

No. of patients	Start of erections (after hospital discharge)	Normal (satisfactory)	Weak (unsatisfactory)
12	1-2 weeks	9	3
17	2 – 6 weeks	7	10
4	6 weeks >		4
Total 33		16	17

Results of the Follow-up: No patient has been lost for follow-up. For 37 patients (out of 40), there were no clinical or radiological evidence of local or nodal recurrence of the disease till the end of their follow-up periods. None of the patients developed distant metastasis. Three patients out of 40 (7.5%): One with normal erection, one with weak erection, and one with no erection, developed clinical and radiological evidence of local recurrence of the disease. In these three patients, the site of local recurrence (as evidenced by pelvic CT) was central in the tumor bed related to the anterior rectal wall, these patients were having positive iliac lymph nodes and grade three tumors. These three patients were subjected to palliative radiation therapy and chemotherapy, but they died due to the recurrent disease at 38, 53 and 75 months after surgery. Another three patients out of 40 (7.5%) died from causes other than cancer and they were remaining free of cancer till their last follow-up visits; from whom one patient (with no erection) died from hepatic failure at 113 months after surgery, and two patients (with weak erection) died from

renal failure at 115 and 130 months after surgery. Out of sixteen patients with normal satisfactory erection following surgery, only 12 patients maintained satisfactory erection up to 10 years. The other four patients: one died from local recurrence at 38 months after surgery, and three patients (one at the 7th year and two at the 10th year) showed gradual weakness of erection and were helped by Sildenafil to reach a satisfactory erection. Out of 17 patients with weak erection following surgery, who were already helped by Sildenafil, one patient died from local recurrence at 53 months after surgery and two patients died free of cancer from renal failure at 115 and 130 months after surgery. Three patients (one in the 7th year and two in the 9th year) developed chronic prostatitis affecting their potency and were treated by antimicrobial drugs and were helped by another supportive pharmacological aid to have a satisfactory erection. Another three patients (at the 10th year) showed gradual and progressive weakness of erection inspite of pharmacological support and at the end of the study they became unable to do a satisfactory relation, these three patients were above 70 years old. The patients with weak erection were helped by Sildenafil and other pharmacological drugs to have a satisfactory erection, (Table 3).

At the end of 10-Year follow-up period (the median follow-up period was 138 months with a range of 109-168): 34 (85%) patients were alive and free of cancer from whom 26 (65%) patients were potent and eight (20%) patients have lost their erectile function. Out of 40 patients 26 (65%) were potent from whom 12 (30%) had normal satisfactory erection and 14 (35%) had weak erection and were helped with Sildenafil. Three patients out of 40 (7.5%) died from local recurrence of the disease at 38, 53 and 75 months after surgery; while another three patients (7.5%) died from causes other than cancer at 113, 115 and 130 months after surgery.

Table 3. Mortality and quality of erections during the follow-up periods for 40 patients.

Follow-up period	Death	Free patients		
		Normal erection	Weak erection	No erection
3 Years Median was 53 months (range : 25 -84)		16	17	7
5 Years Median was 78 months (range : 49-108)	1 (with normal erection) at 38 months (died from local recurrence) 1 (with weak erection) at 53 months (died from local recurrence)	15	17	7
7 Years Median was 102 months (range : 73-132)	1 (with no erection) at 75 months (died from local recurrence)	14	17	6
10 Years Median was 138 months (range : 109-168)	1 (with no erection) at 113 months. (died from hepatic failure) 2 (with weak erection) at 115,130 months (died from renal failure)	12	14	8
Total out of 40	6	12	14	8
Percentage	(15%)	(30%)	(35%)	(20%)

DISCUSSION

The surgical technique described in this present work achieved loco-regional control of the disease for the selected forty studied patients up to ten years after surgery. At the end of the 10-year follow-up period, there were 34 (85%) alive patients out of 40, these 34 patients were free of cancer. However, three patients out of 40 (7.5%) developed local recurrence and died from the disease at 38, 53 and 75 months after surgery and their postsurgical specimens had showed positive iliac lymph nodes and grade 3 tumors. One patient died free of cancer, from hepatic failure, and two patients died free of cancer, from renal failure, at 113, 115 and 130 months after surgery which may be attributable to their bilharzial affection. The primary goal of the surgical procedure described in this present work should be a reduction in the morbidity of the standard radical cystectomy without reducing its efficacy as the most effective form of treatment for T_2 bilharzial bladder cancer, so selection of appropriate patients is of a paramount importance. This technique should be restricted to patients in whom their invasive caner is confined to the muscle wall of the bladder (T_2) and not reaching the peri-vesical fat, because when the disease reaches the peri-vesical fat (T_3a, T_3b), the adequate treatment entails complete extirpation of all fibrofatty areolar tissues from the anterior part of the pelvic cavity. This necessitates removal of the endopelvic fascia that harbors the neural fibres of the cavernous nerves (nervi erigents).

In this present work, the technique of standard radical cystectomy as was described by Skinner and Leiskovsky[18] was followed but with some modifications to preserve potency. These modifications were based on certain anatomical considerations. Because the autonomic pelvic plexus lies in a retroperitoneal location beside the rectum 5-11 cm from the anal verge traveling on the lateral surface of the rectum, and after providing branches to the bladder, lower ureter and prostate, the branches from the pelvic plexus travel in association with the capsular branches of the prostatic artery dorso-lateral to the prostate were the nerves exit to innervate the corpora cavernosa.[6,9,22] So, in this present work, during performing posterior dissection of the bladder no dissection was done deeper than the anterior wall of the rectum in order to avoid injury to the autonomic pelvic plexus which lies on the lateral surface of the rectum.

Because the inferior vesical artery acquires condensations of areolar tissue to enclose it (named the dorso-lateral ligament of the bladder). This ligament encloses vesical veins, inferior vesical artery and lymphatics together with the nerves of the bladder.[22] The branches of the inferior vesical artery and vein that supply the bladder and prostate perforate the autonomic pelvic plexus and the neural fibres scaffold the branches of the inferior vesical artery to reach its final destination.[9] The neurovascular bundle (neural fibres of cavernous nerves) are located within the envelope of visceral prostatic endopelvic fascia adjacent to the posterolateral aspects of the prostate bilaterally.[22] In this present work the inferior vesical artery was protected and the dorso-lateral ligament of the bladder was left undisturbed; Only the branches that supply the bladder were individually ligated very close to the bladder and the same were done for the branches which supply the seminal vesicles. The maintained branch of inferior vesical artery (the prostatic artery) was preserved and not disturbed. The distal two thirds of the prostate with the covering endopelvic fascia were left undisturbed and hence the neural fibres to corpora cavernosa were spared any dissection or interruption during their pathway at the dorso-lateral aspect of the prostatic capsule and at the apex of the prostate where it remained undisturbed.

Throughout the present surgical procedure, the neural fibres that will supply the corpora cavernosa were protected, and were not disturbed and remained intact.

This technique described herein resulted in preservation of potency in 33 (82.5%) out of 40 patients after surgery , from whom 16 (40%) patients were with normal satisfactory erection and 17 (42.5%) patients were with weak erection who were helped by Sildenafil tablets to reach a satisfactory erection . At the end of the 10-Year follow-up period there were 12 (30%) patients with normal satisfactory erection and 14 (35%) patients with weak erection who needed to be helped by Sildenafil or other pharmacological support to reach a satisfactory erection .In the mid-1990s , many surgical techniques for sexual function sparing cystectomy, variously ,based on preservation of the neurovascular bundles , seminal vesicle, vas deferens and prostate capsule were published .Horenblas and his colleagues,[11] Vallancein and his colleagues,[12] Muto and his colleagues[15] and Salem[16,17] described a high rate of potency preservation and a high rate of loco-regional disease control and the results of the present work are comparable to their published results .

Brendler and his colleagues[23] reported 27 (64%) to be potent out of 42 patients, underwent nerve sparing radical cystoprostatectomy, and erections started few months after surgery. In their technique retrograde dissection of the prostate may result in excessive mobilization of the cavernous nerves. Colomo and his colleagues[14] reported all patients (27 patients stage T_1-T_2) to be potent after nerve and seminal sparing radical cystectomy. They used a surgical technique with the least mobilization of the prostatic capsule and the cavernous nerves. They reported that few patients were helped by Sildenafil citrate to improve erection. Sildenafil needs intact nerves to work.[24] There were no recent publications on the issue of nerve sparing radical cystectomy in the recent literature, and the recent publications in the last decade ,the era of laparoscopic or robot-assisted laparoscopic surgery, concerning nerve sparing cystectomy only described laparoscopic techniques that concentrated on the value of nerve sparing procedures for day and night urinary continence

after orthotopic neo-bladder urinary diversion and ignored assessment of potency.

In the present work only 3 patients (7.5%) developed local recurrence of the disease and this may be attributable to that the studied patients were bilharzial, having stage pT2 of the disease and most of the patients were with low grade tumors and all were treated by radical surgery. Tumor stage, grade and nodal status are the only factors which have a significant impact on survival after adequate radical surgery for bladder cancer.[25]

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