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Survival up to 5–15 years in young women following genital sparing radical cystectomy and neobladder: oncological outcome and quality of life. Single–surgeon and single–institution experience

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Introduction This is an observational retrospective study utilising long term patient follow–up for 15 years to determine the survival and quality of life in women (age range 20–54 years) after having been treated for carcinoma of the bladder by radical cystectomy with preservation of genital organs.

Material and methods The study included 13 female patients with urothelial carcinoma of the bladder treated with genital sparing radical cystectomy during the period of 1995 until 2006. They had orthotopic ileal neobladder. Follow–up included recurrence–free survival, metastases–free survival, overall survival, continence, and sexual function.

Results Genital sparing cystectomy was done in 13 women. Seven women were between the ages of 20–37, and 6 women were aged 38–54. Overall survival of 10–15 years was 61.53%, survival from 5 to 9 years was 38.46%. The procedure was done in 9 women with a muscle–invasive tumor of stage T2– T3a. Non–muscle invasive T1 tumor was present in four patients. Quality of life was assessed by continence, which was good in 10/13 patients. Three women needed CIC. Sexual function was tested by female sexual function index >20–30 and was scored at 84.61%.

Conclusions The study provides evidence of safety and efficacy of radical cystectomy with sparing of genital organs in women aged 20 to 54 with urothelial carcinoma of the bladder. Oncological outcome for 5–15 years was good; continence and sexual function were good. This procedure should be considered when surgical approach appears to be feasible. The limitation of our findings is the small sample size of this case series.

Key Words: bladder carcinoma ‹› cystectomy ‹› survival ‹› genital–sparing ‹› women ‹› quality of life ‹› sexual function ‹› continence

INTRODUCTION

In female patients, the standard treatment for invasive carcinoma of the bladder is anterior pelvic exenteration including the bladder, anterior vagina, uterus, distal ureters, ovaries, fallopian tubes, and representative lymph nodes. In cases in which the tumor is not in the bladder neck area or in the urethra, it is indicated to preserve the urethra and to perform an orthotopic neobladder [1]. Cystectomy for non–muscle–invasive bladder cancer is considered for patients who are at high risk of progression. These patients have multiple recurrences, high grade T1, T1 patients with concomitant CIS, and/or failed BCG. Delayed cystectomy in this category would lead to diminished disease–specific survival [2]. There are previous reports on genital sparing cystectomy with preservation of genital organs and the construction of orthotopic ileal neobladder [3, 4, 5].

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There is cumulative data questioning the necessity of removing a long portion of the anterior vaginal wall, where orthotopic neobladder was possible in women with good oncological and functional outcome [6–9]. This study is aimed at examining the survival up to 5–15 years, with analysis of oncological and functional outcome in 13 young women undergoing genital sparing radical cystectomy and orthotopic ileal neobladder.

MATERIAL AND METHODS

Study design

Between 1995 and 2004, thirteen female patients underwent radical cystectomy (RC) with preservation of genital organs and orthotopic ileal neobladder urinary diversion. The female genital organs that were preserved were the entire vagina, uterus, fallopian tubes, and ovaries. All patients were informed of the detailed procedure and provided informed consent, and the study was approved by the ethics committee. Inclusion criteria were urothelial carcinoma of stage T1 tumours that were recurrent, of high grade, as well as failed BCG therapy, with no concomitant CIS. Muscle–invasive urothelial carcinoma of T2 and T3a were included in the series provided that the tumor was completely removed by trans–urethral resection and was away from the trigonal area and the urethra. In all cases, there were no associated CIS or dysplasia in the rest of the bladder, which was confirmed by mapping histology of the bladder on cystoscopy. Abdominal ultrasonography and CT– urography showed that the tumor was localised to the bladder, had no perivesical fat extension and was not at T3b or T4 tumor stage.
Vaginal examination and vaginal ultrasonography showed no tumours or papilloma in the cervix uteri, no detectable diseases of the uterus and ovaries. Five women out of the 13 were not married, and were wishing to have a normal marital life when getting married, and approved the procedure of genital sparing cystectomy. Age range was 20–28 years (mean 24 years) in four women 4/13 (30.77%), three women 3/13 were of age range 32–37 (mean 35 years). Six women 6/13 of age range 42–54 (mean 48.5 years).

Surgical procedure

Patients underwent urethro–cystoscopy to localise the urethro–vesical– junction (UVJ). To identify the UVJ during cystectomy, a cystoscopic injection needle was used and guided by the Alberan bridge and 30° optical telescope to inject 0.5 ml methylene blue solution in the positions 12, 3, 6, 9 in the region of the UVJ. An indwelling urethral catheter was passed to the bladder and filled with 10 ml saline solution. An infra–umbilical incision was done, lymphadenectomy on both sides included iliac lymph nodes below the bifurcation of the common iliac vessels to the end of the external iliac vessels as well as obturator lymph nodes with clearance of the obturator fossa. The ureter was identified and followed down to the crossing of the superior vesical vessels that were ligated and divided close to the bladder wall. Further down, the inferior vesical vessels were ligated and divided close to the bladder wall. The ureters were divided at the level of the uretero–vesical junction. Lateral ligaments of the bladder were divided close to the bladder wall. The bladder was turned interiorly to get access to the vesico–uterine peritoneal reflection that was opened and sharp dissection was performed to reach the posterior bladder, trigonal area. Opening the vesico–uterine and vesico–vaginal spaces with sharp dissection would separate the posterior bladder wall from the anterior vaginal wall (Figure 1). The blue colour of the methylene blue previously injected in position 6, 3, 9 of the UVJ would be the landmarks where the bladder would be removed in the posterior level. The bladder was pushed posteriorly and careful dissection was made in the retro–pubic space

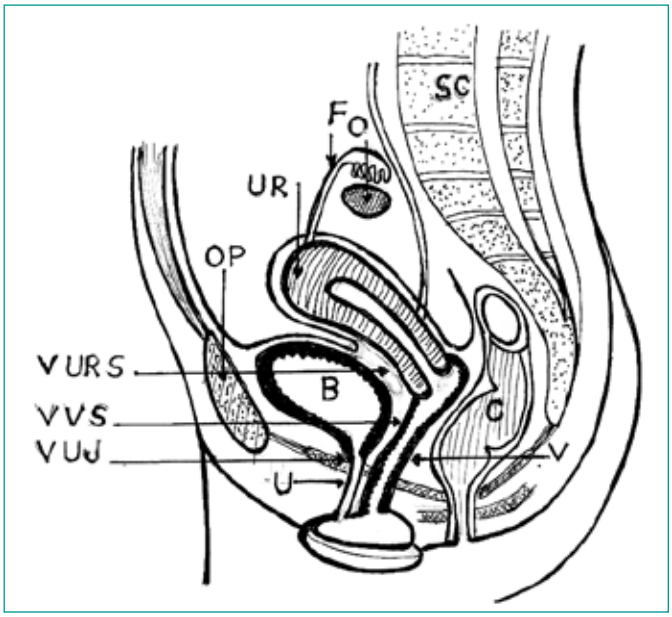

Figure 1. *Anatomy of the female pelvis with relations of the urinary bladder to the female genital organs. It shows the surgical anatomy: vesico–uterine space, vesico–vaginal space, and urethro–vesical–junction.*
B: bladder, UR: uterus, U: urethra, V: vagina, O: ovary, F: fallopian tube, C: colo–rectum, Sc: sacrum, VURS: vesico–uterine space, VVS: vesico–vaginal space, VUJ: vesico–uretheral junction.

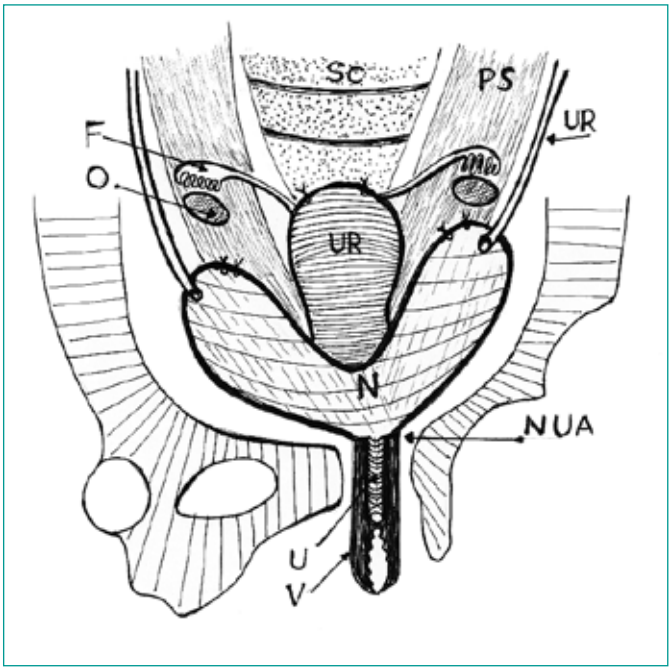

Figure 2. *Final view of the procedure of female genital sparing cystectomy with construction of U shaped orthotopic ileal neobladder. It illustrates the anchoring sutures between the uterus and the pre–sacral fascia, as well as the anchoring sutures of the horns of the U shaped ileal neobladder to the psoas muscle fascia.*
N: neobladder, UR: uterus, U: urethra, V: vagina, O: ovary, F: fallopian tube, Sc: sacrum, PS: psoas muscle fascia; NUA: neobladder urethral anastomosis.

to reach the anterior portion of the UVJ (Figure 1). The bladder was separated from the UVL after application of a vascular clamp following deflation of the balloon catheter. The ileal neobladder was constructed as a U shaped detubularised pouch. The ureters were anastomosed to the ileal pouch by the direct dipping technique. The ileal pouch was anastomosed to the urethra with four interrupted 3/0 polyglycolic acid sutures. The two ureters were drained externally via two ureteral stents, the bladder was drained with an 18 F silicone Catheter, which was anchored to the anterior abdominal wall with a Harris stitch to guard against slipping of the indwelling catheter if the balloon was accidently deflated, and to avoid pressure on the anastomotic site between the ileal pouch and the urethra. The uterus was fixed to the peri–sacral periosteal fascia and the two horns of the U shaped ileal neobladder were anchored to the iliopsoas fascia on either sides. These fixation steps were done to prevent anterior angulation of the neobladder with subsequent acute angulation of the neobladder–urethral anastomosis that may lead to hypercontinence (Figure 2).

Follow–up

Patients were seen in the outpatient clinic as follow–up 3 months, 6 months, 12 months and then annually. Oncological Assessment: Each visit work–up was done for local recurrence and metastasis. Work–up included: Abdominal ultrasonography, urine cytology, CT urography, annual cystoscopy, chest and abdominal radiograph. Follow–up included disease–recurrence and/or metastasis, cancer–specific mortality. Overall survival was calculated from the time of operation to the cut– off date of the study (mid 2014).

Quality of life

1. Continence. Continence was defined as the use of one or no pads per day. Each patient level of continence was evaluated at the follow–up visits. Evaluation of continence was made according to the Sandvik severity score [9]. Urodynamic was done annually.
2. Instrumentation need. Women who had hypercontinence were instructed to perform clean intermittent catheterisations (CIC) five times per day and once by night.
3. Sexual Function. Sexual function was assessed using the female sexual function index (FSFI) [10], after 6 months from the date of the operation. The FSFI questionnaire is a brief self–reporting measure of female sexual function structured in six domains: desire, subjective arousal, lubrication, orgasm, satisfaction, and pain, with scores ranging from 3 to 36. The FSFI has the validity of distinguishing women with sexual dysfunction from normal.

RESULTS

Demographic data

Details of the 13 patients are in table 1. Age distribution was as follows: patients between 20 and 28 years (mean 24 years) were 4/13 (30.77%). Women of age range of 32–37 (mean 35 years) were 3/13 (23.07%). Women of age range of 40–54 (mean 49 years) were 6/13 (48.5%).

Clinocopathological distribution

All tumours were urothelial carcinoma; stage T1 were 4/13 (30.77%), stage T2 were 5/13 (38.46%), stage T3a were 3/13 (23.07%). The grades of the tumours were G1 2/13 (15.38%), G2 10/13 (77%), G3 1/13 (7.69%). Surgical margins of the lower ureters and the trigonal area were negative for carcinoma in situ or dysplasia.

Table 1. *Demographic data of patients, survival, and quality of life of women treated with radical cystectomy with preservation of genital organs and had up to 15 years survival*

Patient I.D	Demographics				Survival			Quality of life		
	Age yr	pT stage	Grade G1–3	TNM stage	Recurrence – free survival ys	Metastases – free survival ys	Overall survival ys	Continence	Sexual function FSFI	Instrument support (CIC)
1	20	T2	G2	T_2N0M0	15	15	15	Good	30	No
2	25	T1	G2	T_1N0M0	15	15	15	Good	32	No
3	32	T1	G2	T_1N0M0	13	13	13	Good	28	No
4	36	T2	G1	T_1N0M0	10	10	10	Good	25	No
5	42	T2	G2	T_2N0M0	12	12	12	Good	33	CIC
6	37	$T3_a$	G2	$T_{3a}N0M0$	7	7	7	Good	30	No
7	52	T2	G3	T_2N0M0	5	5	5	Good	20	No
8	53	T1	G1	T_1N0M0	15	15	15	Good	0	No
9	28	T2	G2	T_2N0M0	15	15	15	Good	32	No
10	45	$T3_a$	G2	$T_{3a}N0M0$	5	6	6	Fair	20	CIC
11	54	$T3_a$	G2	$T_{3a}N0M0$	7	7	8	Good	15	No
12	23	T2	G2	T_2N0M0	14	14	14	Good	21	CIC
13	45	T1	G2	T_1N0M0	9	9	9	Good	22	No

Female Sexual Function (index FSFI), ranging from 2 to 36

Survival

It was evaluated as overall survival and disease–free survival. 8/13 women (61.53%) survived up to 10–15 years. 38.41% survived for 5–9 years (5/13). Women who are still alive in the year 2014 and are in good health with no evidence of disease recurrence or metastases equals 4/13 cases (30.77%); they are numbers 1, 2, 8 and 9 in table 1. Two of these four women had tumor stage T1, the other two were stage T2. Two were G1 and the other two were G2. Their age at the time of surgery was 20, 25, 28, and 53 yrs.

Sexual function

It was estimated according to FSFI. Women who had reported good sexual function had DSFI score ranging from 20 to 32, which was reported by 11/13 cases (84.61%). One woman had a score of 15, while another woman was not married and had no partner and she reported a score of zero.

Continence

Nine women (9/13) were continent (69.23%). Four women (4/13) (30.76%) were on CIC. Urodynamic examination of continent women on the annual follow–up showed that the neobladder capacity was mean of 315 ml (range 280–375), mean maximum urethral closure pressure was 22.6 ±8.2 cm H_2O, for a mean flow rate of 21.9 mi/s. Patients who had post–void residual over 100 ml were categorised hyper–continent and had regular CIC.

DISCUSSION

This work is an observational retrospective study for 15 years, examining survival and quality of life in 13 women of ages between 20 and 54 years (mean 37 years). Our results are compatible with the results of other published works of genital sparing radical cystectomy in women [3, 4, 5]. The work of Koie et al. [5] where they spared the uterus, fallopian tube, and ovary during cystectomy followed by U–shaped ileal neobladder in 30 women treated for carcinoma of the bladder, had a follow–up of 35.7 months. One patient had early local recurrence and another 6 patients had recurrence. They recommended that orthotopic neobladder reconstruction with preservation of gynaecologic organs is feasible for female bladder cancer patients. They recommended this technique as it provided an acceptable oncological outcome and good voiding function. When comparing our results to Koie's, we had 8 patients with survival up to 10–15 years. Four women had long survival up to 15 years and on.

Nunnk et al. [3] reported 2 cases of women undergoing sexuality–preserving cystectomy for urothelial

carcinoma of the bladder. These two women were 33 and 28 years, they became pregnant and had healthy children. In our series, no woman became pregnant although they reported high index of sexual function in 84.61% in their follow–up after genital sparing cystectomy

Ali–El–Den et al. [4] reported 15 cases of women undergoing genital–sparing cytectomy. 2 patients developed local recurrence and metastasis after 4 months of the procedure, another patient developed metastasis after 15 months. They reported 12 patients who survived for 15 months and were continent. They reported that sexual function in this group was better than those who had not had genital–sparing cystectomy. In the present work, we reported 10–15 years survival, and good functional, and oncological outcome. The result of this work of long disease–free survival in early cystectomy in low stage, low grade urothelial tumor emphasises the previous work of others [2] who advocated cystectomy in superficial urothelial carcinoma, as delayed cystectomy in these patients may lead to decreased disease–specific survival. In the present study, four patients (30.77%) were of stage T1, G1–2, and their survival was within the range of 9–15 years.

Limitation of the present study is the lack of randomisation of patients. The good oncological and functional results might be bias introduced by the high selection of patients.

CONCLUSIONS

This study provides strong evidence of safety and efficacy of female genital organ sparing cystectomy in young women. The oncological and functional outcome including continence and sexual life were excellent. This procedure should be considered in highly selected women patients where surgical approach is feasible. This procedure is of significant value for young women who developed invasive carcinoma of the bladder with low stage and low–grade tumours.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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