

Functional outcome improvement with Studer's orthotopic Neobladder after radical cystectomy, 10 years' experience

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Abstract: The objective of this study was to retrospectively study the feasibility and results of Studer's orthotopic bladder in the last decade. We retrospectively identified 39 patients who underwent Radical cystectomy and Studer's Orthotopic Neobladder in South Egypt Cancer Institute (SECI) for the period January 2004 to January 2014. We evaluated oncological and functional outcomes—peri-operative and late complications. **Results:** There were 39 patients (37 men and 2 women) studied in total. The median age was 55 years. Median operating time was 315 min. Median blood loss 1000 ml. Median hospital stay was 14 days. Bilateral nerve sparing in 25 patients (64.1%). Seminal sparing in two patients (5.1%). Early complication in 12 patients (30.8%). Late complication in 8 patients (20.5%). Overall 5-year survival was 28 patients (71.8%). Overall cancer-specific mortality was 6 patients (15.4%). Surgery-related overall mortality was 2 patients (5.1%). Overall recurrence rate in 6 patients (15.4%), with local pelvic recurrence in two patients (5.1%) and distant metastasis in 4 patients (10.3%). 27 patients (69.2%) patients received adjuvant chemotherapy. 26 patients (66.7%) patients received adjuvant radiotherapy. Pathological TNM staging; IIA, IIB, IIIA, IIIB, IVA was 4 patients (10.3%), 4 patients (10.3%), 14 patients (35.9%), 3 patients (7.7%), 14 patients (35.9%), respectively. Continence after 6 months; Day-time, Night-time were 33 patients (84.6%), 18 patients (46.2%), respectively. Continence after 1 year; Day-time, Night-time were 36 patients (92.3%), 35 patients (89.7%), respectively. Ability to empty in 36 patients (92.3%). The radiological evaluation in each patient were revised; the oncological outcome were revised with RECIST criteria (version 1.1) while the bladder capacity and postmicturition residue were calculated by prolate ellipsoid equation. Median bladder capacity after 6 and 12 months were 320mL and 480mL, respectively. Median residual urine after 6 and 12 months were 30mL and 15mL, respectively. **Conclusion:** Studer's Orthotopic Neobladder is a safe and effective option for urinary diversion in selected patients with good oncological and functional outcomes, and has an acceptable early and late complication rate.

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I-Introduction

Radical cystectomy with bilateral pelvic iliac lymphadenectomy is the gold standard treatment for high-grade, muscle-invasive bladder cancer^{1,2}. Studer's Orthotopic Neobladder was described in 1984, will maintain the largest capacity with the lowest pressure uses, a long, afferent, iso-peristaltic, tubular ileal segment has been demonstrated to prevent reflux by transmission of intra-abdominal pressure, less metabolic consequences, simplicity of the construction, ability to accommodate short ureter, provides unchanged voiding habits with good continence and upper urinary tract preservation, with relatively low rates of complication²⁻⁶. The intact voiding function is attributed to preservation of autonomic nerves and subsequent preservation of sexual activity in both sexes^{7, 8}. Among the contraindications of Studer's Orthotopic Neobladder are severe hepatic, renal and intestinal dysfunction, positive margin status of the urethra, recurrent

urethral stricture, and urinary stress incontinence, and damaged rhabdo-sphincter, physical and mental impairments. Patients with comorbidities are often recommended for conduit diversion^{3, 4, 7}, patient age, locally advanced tumor stage or limited lymph node tumor are not necessarily a contraindication for Studer's Orthotopic Neobladder^{9, 10}.

2-Methods

We retrospectively identified 39 patients who underwent Radical cystectomy and Studer's Orthotopic Neobladder in South Egypt Cancer Institute, Assiut University¹¹ from January 2004 to January 2014. Patient data analyzed were gender, age, operative data regarding operative time, estimated blood loss, Lymph nodes. Length of hospital stay and Peri-operative complications; early (3 months or less) or late (after 3 months), oncological and functional outcome

I-Surgical technique

Standard radical cystectomy bilateral pelvic lymph node dissection was performed. Adequate urethral stump was left. Studer type neo-bladder was constructed by isolating a 60 cm segment of small bowel approximately 20 cm proximal to ileo-cecal valve.

The distal 40 cm of this segment was opened at the anti-mesenteric border and it was made into a spherical reservoir consisting of four cross-folded de-tabularized segments 3 - 0 braided polyglactin (vicryl). A direct uretero-ileal anastomosis was carried out bilaterally over a feeding tube via an end-

side fashion on the afferent iso-peristaltic segment which functions as an anti-reflux mechanism to protect the upper urinary tract.

The reservoir was anastomosed over its most dependent part by approximating about 8 mm hole with Urethral anastomosis at the most dependent part of the neobladder was performed over a 20-22 Fr 3 ways silicon urethral catheter. The ureteral catheters were removed on the 15th postoperative day. On the 21st postoperative day, the urethral catheter was removed afterwards. [some operative images illustrated in [figure (1)]]

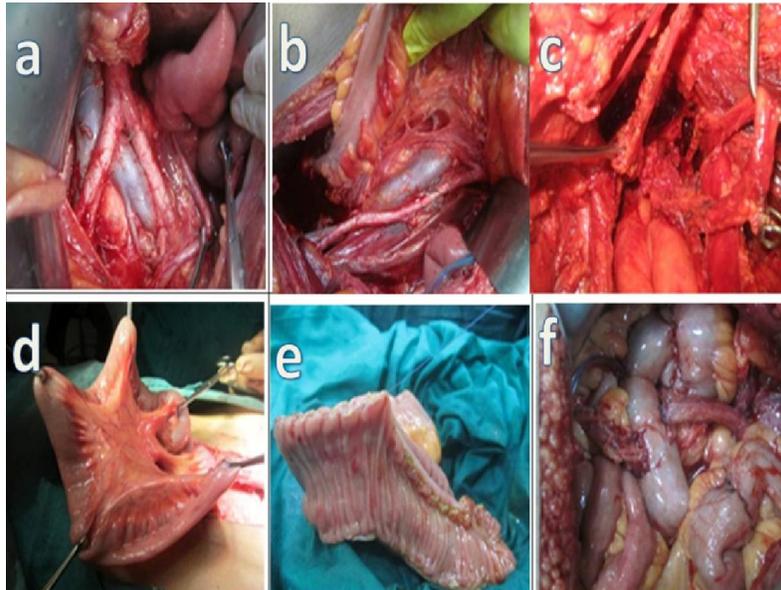


Fig (1) different operative photo series where (a) shows Extended pelvic lymph node dissection (in order to reach the origin of inferior mesenteric artery) ,(b) shows pelvic lymph node dissection, (c) Seminal sparing Radical cystectomy, (d) 60cm ileal segment is isolated about 20-25 cm proximal to the ileo-cecal valve, (e) 40cm of the distal ileal segment is then detubularized on the anti-mesenteric border (f) Spherical shape reservoir consisting of four cross-folded ileal segments. The ureters were next anastomosed to the afferent tubular segment in end-to-side fashion

II-Patient follow up

Oncological and functional follow-up included Clinical, Laboratory and imaging assessments ;Our patients were followed regularly every 3 months for 2 years, every 6 months for next 3 years and then at yearly intervals thereafter. The evaluation was done by clinical history, physical examination, urinalysis and culture sensitivity, blood chemistry and imaging by abdominal ultrasonography and with abdominopelvic CT scan and CT chest from 2012 MDCT of abdomen and pelvis. We do not have urodynamic evaluation device at our institute so we depend on oncoradiology department on measurement functional results. Median follow up was 28 months (from 13 -102 months).

Evaluating the Functional outcome [regarding the Capacity, Continence status, Voiding pattern, difficulties ,Residual ,Metabolic , Upper tract status

and sexual activity] and Oncological out-come , regarding the oncological output RECIST criteria version 1.1 were applied while for the functional output regarding the capacity of UB the prolate ellipsoid equation were employed as $\text{volume} = \text{length} \times \text{width} \times \text{height} \times 0.52$ were applied¹². [This is clearly demonstrated as in figure (2)] .where the 3rd dimension were calculated on the MDCT images due to its isotropic properties while in conventional CT the 3rd dimension is estimated from the number of cuts and slice thickness. On the other hand the postmicturation residue was calculated from sonography images by the prolate ellipsoid method or that which is routinely recorded in the sonography reports.

Minimum follow-up included in the study were one year,

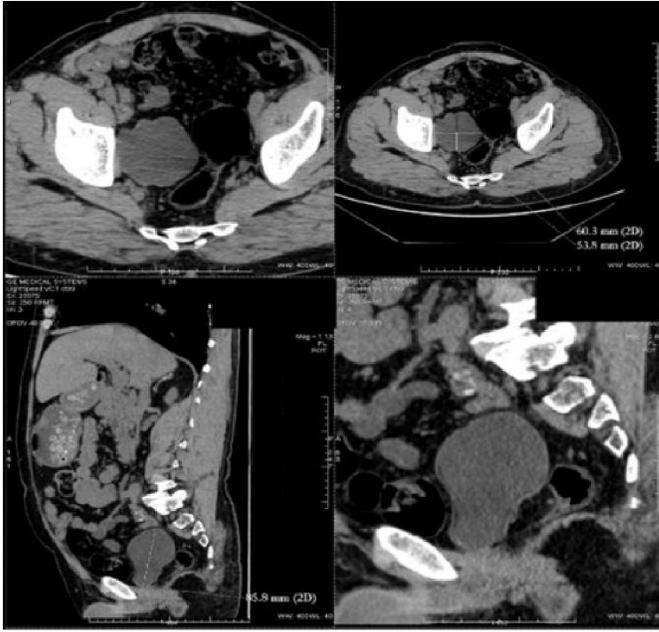


Fig (2) calculation of the capacity of the neobladder by prolate ellipsoid equation from MDCT series with capacity is estimated to be 138 cc in this case

Statistical methods:

All analyses were done using SPSS® (Statistical Package for Social Sciences) software, version 21, IL, Chicago, USA. Numerical values were expressed as means or medians and standard deviation (SD) or range. Survival was estimated using Kaplan Meier methods. Curves were compared using log rank test. Relations between categorical variables were assessed using the Chi-square / Fisher Exact tests.

3. Results

In total, 39, patients radical cystectomy and Studer's Orthotopic Neobladder were identified in 37 men and 2 women. The median age was 55 years (17-74), The median Operating Time was 315 min (275-420), Blood loss was 1000 ml (650 -1850), Median of hospital stay was 14 days (7 -23), Mean number of Lymph nodes removed was 16 (range, 5-28), Bilateral nerve sparing was performed in 25 patients (64.1%) , Seminal Sparing in two patient (5.1%). Early complication in 12 patients (30.8%) where 2 patients (5.1%) had surgical site infection, 2 patients (5.1%) had pyelonephritis, 1 patients (2.6%) had urinary leak /fistula, 2 patients (5.1%) had ileus/bowel obstruction, 2 patients (5.1%) had hyperchloremic acidosis electrolyte imbalance, 2 patients (5.1%) had pneumonia, 1 patients (2.6%) had deep venous thrombosis while Late complication occur in 8 patients (20.5%), two patient (5.1%) developed Wound hernia , bowel obstruction in one patient (2.6%), renal deterioration increased serum kidney functions, dilatation of upper urinary tracts occur in 5 patients (12.8%) as 3 patients (7.7%) had recurrent pyelonephritis, 1 patients (2.6%) had

urinary stones ,1 patients (2.6%) had Urinary retention

Chemotherapy given to 27 patients (69.2%). Radiotherapy given to 26 patients (66.7%). Pathological staging with TNM staging system were IIA, IIB, IIIA, IIIB, IVA 4 patients (10.3%), 4 patients (10.3%), 14 patients (35.9%), 3 patients (7.7%), 14 patients (35.9%) respectively . Tumor Grade differentiation High, Low in 26 Patients (66.7%), 13 patients (33.3%) respectively. Continence defined as 0-1 pads per day, after 6 months {Day-time 33 patients (84.6%), Night-time 18 patients (46.2%)}, after 1 year {Day-time 36 patients (92.3%), Night-time 35 patients (89.7%)}. Ability to empty completely 36 patients (92.3%). the bladder capacity and postmicturation residue were calculated by prolate ellipsoid equation. Mean bladder capacity after 6, 12 months (320,480ml), Mean residual urine after 6, 12 months (30,15ml) [Table 1].

Sexual life 7 patients (17.9%), reported unaltered sexual desire the "very much" decrease in sexual desire 9 patients (23.1%) Erectile dysfunction occurred in 34 patients (87.2%) of sexually active men, 18 patients (46.2%) retained adequate erectile function satisfaction with the diversion was described as "poor" by 9 patients (23.1%), "good" by 22 patients (56.4%), "very good" by 8 patients (20.5%) Overall 5-year survival was 28 patients (71.8%), overall cancer-specific mortality was 6 patients (15.4%) and surgery-related overall mortality was 2 patients (5.1%) . Overall recurrence rate in 6 patients (15.4%) as Local pelvic recurrence occur in two patient (5.1

%) [figure 3] while four (10.3%) had Distant metastasis in (liver, lung, bone)}.

Table (1): showing orthotopic neobladder capacity and post voiding residue after 6 and 12 months.

	N	Mean	±Std. Deviation	Median	Minimum	Maximum
bladder Capacity/ml after 6 months	39	336.41	38.302	320.00	280	410
bladder Capacity/ml after 12 months	39	476.41	39.101	480.00	370	530
Residual Urine/ml after 6 months	39	33.33	17.447	30.00	10	80
Residual Urine/ml after 12 months	39	15.95	6.731	15.00	5	30



Fig (3) patient with local pelvic recurrence with infiltration of pelvic floor muscles, left internal obturator muscles and gluteal muscles with infiltration of iliac bone ...recurrence detected after 7 years from the operation. Patient was referred to radiotherapy.

4. Discussion

Studer's Orthotopic Neobladder provides the largest capacity of all reservoirs, this capacity provides the improved voiding pattern and continence.¹⁰ The maximum bladder capacity at 6 months was 384 ± 66 (290 - 520) mLs, one year was, 484.1 ± 119.2 mL.^{3, 13} in our study The median bladder capacity after 6 months was 320 ml (280-410), after 1 year was 480 ml (370-530). This large capacity results from refashioned spherical reservoir with a large radius from detubularized bowel enabling to contain higher volumes with low intraluminal pressures.

Voiding dysfunction is an essential item that affects the postoperative satisfaction, In our study 36 patient (92.3%) had the ability of complete emptying this may be attributed to following our instruction to the patients when informing them to micturate in sitting position without spasm or bear down in a trial to relax pelvic floor muscles and sphincters followed by using Valsalva's maneuver and if needed lean forward to increase intrabdominal pressure or apply gentle manual pressure over the suprapubic region while we agree with Steer's [14] on stating that incontinence may range from mild stress incontinence to severe incontinence in a small percentage of patients, but complete day-time continence is achieved in 89.5% and 90% of patients with Neobladder,

In our study continence was defined as a state of complete dryness without the need of protective pads, appliances or medications. 33 patients (84.6%) had Day-time continence after 6 months while only 18

patients (46.2%) had night time continence, after 1 year 36 patient (92.3%) had total Day-time continence, and 35 patients (89.7%) had Night-time total continence. Though our continence rates are similar to those reported in the literature [3-12], Our patients had a better night time continence rate. This is because of the relative younger age of patients in this cohort. Reported studies⁸.

Have shown that older age especially > 70 years has an adverse effect on night time continence. During the early stages, we advised our patients by frequent neobladder emptying every 2-3 hours in day time and every 3 hours at night to avoid overflow incontinence.

Preservation of autonomic nerves supplying the remnant urethra Nerve sparing improve the continence following Studer's Orthotopic Neobladder A significantly longer functional urethral length and a higher maximal urethral pressure have been observed in nerve preservation⁸.

In our study bilateral nerve sparing surgical approaches in 25 patients (64.1%) among them 18 patients (46.2%) retained adequate erectile function. Such frequency coincided with that previously reported in literature between 23.7-35.5% of patients retain adequate erectile function after neobladder reconstruction.⁸

In a large series with a follow-up of up to two decades Studer *et al.* observed residual urine volumes of more than 100mLs in 22% of all male and female Neobladder patients¹⁴. In our study Median residual urine after 6 month was 30ml (10 - 80), after 12 months was 15 ml (5-30). The mean post-void

residue was very low which reflects the good ability to completely evacuate the neo-bladder.

Sexual activity is strongly correlated with autonomic nerve preservation and potency. Schoenberg et al.¹⁵ reported a correlation between age and potency in nerve sparing cystectomy in a 10-16 year experience moreover Kessler et al.¹⁶ recovery of erectile function was significantly more frequent in younger patients (< 65 years). In our study 7 patients (17.9%), reported unaltered sexual desire, Erectile dysfunction occurred in 34 patients (87.2%) of sexually active men, 18 patients (46.2%) retained adequate erectile function.

Bacterial colonization (strongly associated with residual urine) of Studer's Orthotopic Neobladder occurs in 40-80% of patients, approximately 6% progress to overt pyelonephritis.¹⁵ In our study only (5.2%) had pyelonephritis due to less residual urine. Radical cystectomy with Orthotopic Neobladder is still associated with significant complications. Reported rates and types of complications vary widely 24-48% in the larger series^{3, 17, 18}; in our study 20 patients (52%) had complication

Most early complications including bleeding, neurologic, thromboembolic, cardiac and pulmonary complications, wound-related, gastrointestinal, genitourinary problems and infection are related to urinary diversion (26.2%), Gastrointestinal complications were most common (29%), followed by infectious complications (25%) and wound-related complications (15%).¹⁹ in our study Early complication in (30.7%), Surgical site infection (5.2%), Pyelonephritis (5.2%), Urinary leak /fistula (2.6%), Ileus/ bowel obstruction (5.2%) hyperchloremic acidosis, electrolyte imbalance (2.6%)(die), Pneumonia (5.2%), Venous Thrombosis (2.6%)(develop pulmonary embolism then die).

The primary late reported complications of Orthotopic Neobladder include atrophied kidney, chronic pyelonephritis, decreased renal function, ureteroileal or urethral anastomotic site stricture, urinary tract stones, and incontinence.³ In late complication rate between 11.6% and 23.5% has been reported in different series. 45% of patients in the first 5 years. This percentage increased to 50%, 54% and 94% at 10, 15 and 20 years, respectively. At 20 years, 50% of patients had upper urinary tract changes and 38% had urolithiasis⁷ in our study Late complication occur (20.8%), (5.1%) developed Wound hernia, Bowel obstruction (2.6%) Renal deterioration in (10.3%) {(7.7%) development of recurrent pyelonephritis, (2.6%) had Urinary stones, (2.6%) had Urinary retention, and there was less deterioration of renal function, both structurally and functionally. Explanted by urine usually remains sterile within the closed system of orthotopic

substitute and the dynamic anti-reflux properties of afferent ileal loop prevent reflux nephropathy and structural deterioration and we consider impaired renal function is a contraindication to having a Studer's Orthotopic Neobladder, Good voiding with no or less residual urine, early treatment of any urinary infection, we did not use staples (foreign bodies) so we have only one patient with stone formation

Careful electrolyte balance with meticulous monitoring with sufficient hydration and if needed oral intake of sodium bicarbonate helped to overcome the electrolyte imbalance which is a reported common complication of urinary diversion²⁰ while in our study we faced 2 patients (5.1%) with hypokalemic hyperchloremic acidosis.

Late Mortality in four patient (10.4%) at (25, 37, 41, 48) months from tumor metastases (recurrence in bone, liver, lung two patients).

Overall 5- and 10-year recurrence-free survival in organ-confined disease in contemporary large series is 62-68% and 50-66%, respectively (7) in our study Overall 5-year survival was 28 patients (71.8%) our patients younger age group

Risk factors for tumor recurrence after cystectomy are the presence of tumors at the bladder neck and high grade, overall recurrences in 11%, 14%, 10-12%, 7-12%, 27-43%.^{7, 13, 20-22} in our study Overall recurrence rate in (15.6%) {Local pelvic recurrence in (5.2%), (10.4%) Distant Recurrence in (liver, lung, bone)} this high Recurrence due to high grade tumor (66.7%)

Our study had several limitations. The number of patients in this study was small, which imposed limitations on statistical power. This was a retrospective analysis, which created the potential for selection bias. Further large, prospective investigations and long-term follow-up are required to evaluate the definite conclusions.

Conclusion

Studer's Orthotopic Neobladder produce good functional results, oncologically safe, and technically feasible with acceptable complication rate, and We recommend this form of continent diversion as the preferred option in appropriately selected cases following radical cystectomy.

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