VIP neobladder (Padovana) reconstruction following radical cystectomy for bladder cancer
Complications, functional outcome and quality of life evaluation in 95 cases.

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Nikolaos Kostakopoulos*, Vassilis Protogerou**/***, Andreas Skolarikos*, Ioannis Varkarakis*, Athanasios Papatsoris*, Theodore Troupis**, Maria Piagou**, Charalambos Deliveliotis*

**2nd Department of Urology, Sismanoglion Hospital, Athens Medical School, Athens, Greece*
***Department of Anatomy, Athens Medical School, Athens, Greece.*
****Department of Urology, "Attikon", University Hospital, Athens Medical School, Athens, Greece*

VIP neobladder (Padovana) reconstruction following radical cystectomy for bladder cancer. Complications, functional outcome and quality of life evaluation in 95 cases.

The Authors report a complete study concerning complications, the imaging and functional results, the clinical outcome and the quality of life in patients treated with VIP. 95 patients with localized bladder TCC (T2N0M0) were evaluated. Follow up points were 1st, 3rd, 6th, 12th, 18th, 24th and 36th month with clinical and ultrasound evaluation. At 6th, 12th and 36th month CT pyelography and urodynamic evaluation were performed and we used a questionnaire for subjective bladder function and the EORTC QLQ C-30 questionnaire to evaluate quality of life. Perioperative complications were ileus (2 patients; 2.1%) (Clavien Grade IIIb), one postoperative death (1.0%) (Clavien Grade V) and a resuscitated cardiac arrest (1.0%) (Clavien Grade IVa). Postoperative complications were incisional hernias (n=4 patients; 4.21%) (Clavien Grade I) and hydronephrosis in five patients (5.26%) due to ureteric/neobladder stricture (Clavien Grade IIIb). Urine retention due to neobladder neck stenosis was observed in one patient (1.0%) (Clavien Grade IIIb) and an ileo-neobladder fistula in one (1.0%) patient (Clavien Grade IIIb). During follow up there were two cancer related deaths (2.1%). According to urodynamic evaluations neobladder capacity increased, end-filling pressure and Qmax decreased while residual urine and the number of intrinsic contractions remained stable. Continence rates and quality of life were high and stable during follow up. VIP technique for bladder substitution is a relatively easy technique with low rate of complications, good functional results which respect the patient's quality of life.

KEY WORDS: Bladder cancer, Neobladder, Padovana, Quality of life, Radical cystectomy, VIP

Introduction

Since 1990 when Artibani et al reported the technique for neobladder formation [1] VIP has been used for bladder substitution after radical cystectomy with good results [2-6]. Here, we present, an important number of consecutive patients, a complete evaluation of multiple parameters including radiological and functional urodynamic results as well as the complications and the quality of life patient's outcome during a 36-month postoperative follow-up period.

Material and Methods

95 patients with muscle invasive bladder TCC (cT2N0M0) without any neo- or adjuvant treatment and with preoperative negative prostatic urethral biopsies, underwent radical cystectomy and neobladder formation using the Padovana technique. In no patient any other treatment was used. Postoperative follow up visits were scheduled at one month postoperatively and then at 3rd, 6th, 12th, 18th, 24th and 36th month. At each visit clin-

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Correspondence to: Vassilis Protogerou, 23 V. Laskou str., 11633 Athens, Greece, (e-mail: vassilis_protogerou@hotmail.com)

Appendix 1
Questionnaire of Subjective Functional Evaluation of Neobladder

Do you use catheter to empty your bladder?
– Never
– Once daily
– More than once daily
Do you leak urine during the daytime?
– Yes
– No
If you leak, haw many pads do you use per day?
– One, but for psychological reasons mainly.
– One
– Two
– More than two
Do you leak urine during night?
– No
– Yes
– No, I wake up and go to toilet

ical and ultrasound evaluation as well as serum biochemical test (full blood count, creatinine, urea, Na, K, P, Ca^{++}) were performed. CT pyelography and urodynamic evaluation were performed at the 6th, 12th and 36th postoperative month. Subjective functional evaluation of the neobladder was performed with the use of a questionnaire (Appendix 1) at the same time points.
A quality of life evaluation was also performed with the use of a questionnaire (European Organization for Cancer Research and Treatment of Cancer Quality of Life Questionnaire [EORTC QLQ-C30] [7], at the same visits. This questionnaire measures basic components of Quality of Life common to most malignancies. It incorporates five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea and vomiting), and a global health and quality-of-life scale. There are also single items that assess additional symptoms commonly reported by cancer patients (dyspnea, appetite loss, sleep disturbance, constipation, and diarrhea), as well as the perceived financial impact of the disease and treatment. Physical function questions have a dichotomous response scale (Yes/No) and global QoL response ranged from 1 (very poor) to 7 (excellent). The other questions have a Likert scale responses with four possible options (1=not at all, 2= a little, 3= quite a bit, 4=very much). A linear transformation in a 0-100 scale was used for all scores. Regarding functional and global health and overall QoL, higher values indicate higher (better) and healthier function and better QoL, while for symptoms and single-item scales higher score corresponds to more problems and decreased QoL.

Urodynamic Studies

A 6Fr urethral catheter and a 14Fr rectal balloon catheter were used. Normal saline was used to fill the bladder at a rate of 20 ml/min at maximum filling volume no more than 1000ml and cystometry and uroflowmetry. Parameters measured were maximum neobladder capacity (the filling volume at which leakage or pain occurred), end filling pressure, intrinsic contractions, Qmax and residual volume.
Changes between the follow up visits were evaluated as following: changes in continuous variables were assessed by the General Linear Model and changes in qualitative date were assessed by chi-square test.

Results

Mean patient's age was 67 years (range 42-79) and pathological stage was pT2N0M0 in 90 and pT2N1M0 in 5. Mean operation time was 244 min (range 200-320 min) and mean transfusion rate was 2.2 units of blood (range 1-3 units). Ureteral stents were removed usually on the 6th day. Mean hospital staying was 7 days (range 5-12). Twenty patients left the hospital prior to the removal of the stents if they had adequate bowel mobilization and they returned for the removal of the stents. No patient prolonged his hospitalization due to leakage from the ureteroileal or urethroileal anastomosis.
Perioperative complications included two patients (2.10%) with ileus (Clavien Grade IIIb) that needed reoperation without any other significant complications. One patient died (1.05%) (Clavien Grade V) due to massive pneumonic embolism and one (1.05%) suffered heart arrest (Clavien Grade IVa) while on recovery room immediately postoperatively but he was successfully resuscitated and he recovered completely.
The following postoperative complications were observed: incisional hernias (n= 4 patients; 4.21%) (Clavien Grade I) that did not need any intervention since they were minor and clinical insignificant. There were no metabolic abnormalities and kidney function remained within the normal limits in all patients. Hydronephrosis was observed in 5 patients (5.26%) (Clavien Grade IIIb) due to ureteric/neobladder stricture. The stricture was discovered at the 6th month (n=2 patients), 12th month (n=2 patients) and 24th month (n=1 patient) visit. In the first four patients a pig tail was placed undergrade (n=3 patients) or retrograde (percutaneously; n=1 patient). In all these patients stents remained up to 3 months without any additional problem. On the 5th patient a stent could not be placed necessitating a reposition of the ureter at the "dome" of the neobladder with an open procedure.
In one patient (1.05%), urine retention appeared 18 months postoperatively. Cystoscopy revealed neobladder neck stenosis due to hyperplasia of the endothelium and fibrosis at the urethroileal anastomosis (Clavien Grade IIIb). The stricture was treated with endoscopic resection without any recurrence.

TABLE I - *Urodynamic results*

	3 months	12 months	36 months	p (3 vs 12 months)	p (12 vs 36 months)
Capacity (ml)	445±33	539±55	590±20	0.002	0.012
Residual (ml)	52±4	60±6	69±9	0.08	0.07
End-filling pressure (cm H_2O)	23±4	20±1	15±1	0.012	0.003
Qmax (ml/sec)	19±5	16±1	13±4	0.018	0.035
Intrinsic contractions (n)	4 ± 1.2	4±6.5	5 ± 1.4	0.09	0.07

One patient (1.05%) developed an ileo-neobladder fistula 12months postoperatively (Clavien Grade IIIb). Using an open procedure the fistula was removed along with a small part of the ileus and an end-to-end anastomosis of the intestine was performed. A small part of the neobladder had also to be removed. The patient is well with no any other problems 24 months after the second operation.

Two patients presented disease relapse at 18th and the 24th postoperative month. Both died from disease progression. All other patients remained disease free during the 36 months of follow up.

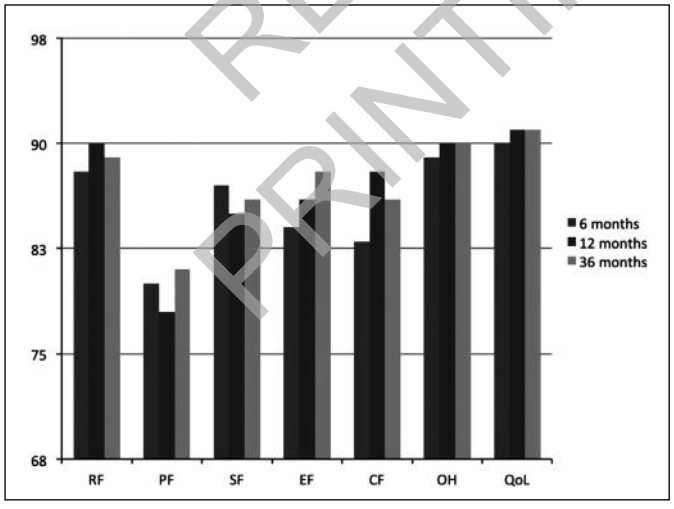
Radiologic evaluation of the patients during follow up revealed the already mentioned hydronephrosis, the ileal-neobladder fistula and the metastasis in the patients that died. In all others patients imagine studies were normal. Serum biochemistry and renal function tests were within normal limits.

Urodynamic evaluations showed that with time neobladder capacity increased. Maximum neobladder capacity at 6th, 12th and 36th month was 445±33, 539±55 and 590±20ml respectively. In all three measurements the difference was statistically significant ($p<0.05$). Residual urine was stable (52±4, 60±6 and 69±9 ml, $p>0.05$ for all measurements). End-filling pressure decreased over time in a statistically significant manner (23±4, 20±1 and 15±1 cm H_2O, $p<0.05$). Accordingly a statistically significant decrease was noted at Qmax (19±5, 16±1, 13±4 ml/sec, $p<0.05$) while on the contrary the number of intrinsic contractions remained stable (4 ± 1.2, 4±6.5, 5 ± 1.4, $p> 0.05$). (Table I)

Eighty-four patients (88.42%) were continent during daytime at the 6th month compared to 85 (89.47%) at 12th and 83(87.36%) at 36th month visit (p=n.s.). Similarly, continence rates during the night were stable with 74 patients (77.89%) being continent at 6 months and 72 (75.78%) and 72(75.78%) at 12 and 36 months respectively (p=n.s.).

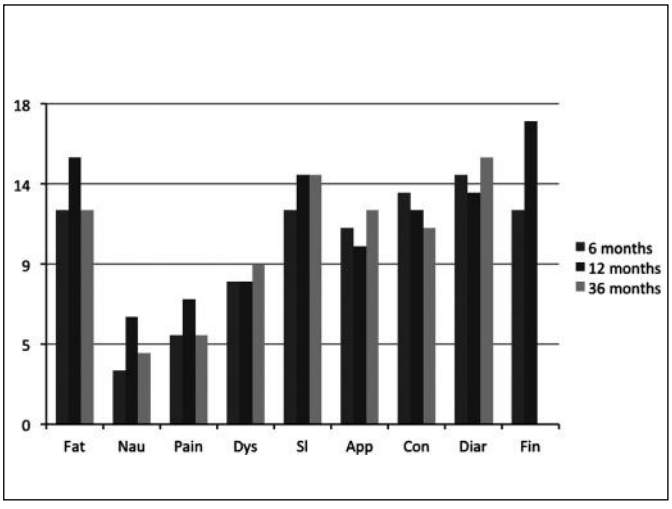
Quality of life results are presented in Table 2 and 3. Overall, there were no statistically significant differences during the follow up period and quality of life was good and stable without changes overtime.

TABLE II - *QoL results.*



Legend: RF: Role Functioning, PF: Physical Functioning, SF: Social Functioning, EF: Emotional Functioning, CF: Cognitive Functioning, OH: Overall Health, QoL: Overall Quality of life.

TABLE III - *QoL results.*



Legend: Fat: Fatigue, Nau: Nausea, Dys: Dyspnea, Sl: Sleep, Appetite: Appetite, Con: Constipation, Diar: Diarrhea, Fin: Finance.

Discussion

Orthotopic neobladder substitution has to fulfill several goals in order to be successful. Good function, tolerability over time and adequate quality of life, related not only to cancer and surgery itself but also to complications or malfunction of the neobladder that can deteriorate everyday life.

In our series complication rate was low and comparable to other orthotopic neobladder techniques [1,3,5,6,8-10].

Ileus rate that needed reoperation is low (2.10%). Death from pneumonic embolism (1.05%) and heart arrest rates are also low and more important they are not related to the reconstruction technique and the VIP neobladder. Neobladder formation can deteriorate renal function and cause metabolic abnormalities. In our patients there were no metabolic abnormalities found not any kidney function deterioration probably because reconstruction of the urinary tract was without significant anatomical alteration that could induce changes in kidney function.

One of the advantages of the VIP neobladder is that it simulates the anatomy of a real bladder with the formation of a trigone and the position of the ureteral orifices on each side. This allows for endoscopic identification of the orifices and if necessary access to the upper tract. In our series four out of five patients with ureteroileal stricture were easily treated with endoscopic placement of a pig tail. Although several treatment options have been described for ureteroileal strictures (balloon dilation, metallic stents, endoureterotomy with cold knife, Holmium laser or Acucise) [11-15] stent placement is an option as described by others [16]. In our patients the use of pig tail proved effective since there was no recurrence in the strictures during follow up. In most severe cases though an open procedures is the best choice therefore in another patient the ureter was reimplanted at the "dome" of the neobladder.

In the patient where an urethroileal stricture occurred, careful endoscopic resection solved the problem without any additional problem. All these manipulations did not compromise the function of the neobladder proving that VIP is very tolerable to additional procedures.

CT pyelography showed a well preserved upper tract without any changes apart the already mentioned hydronephrosis and the neobladder-ileal fistula. In all cases and after all additional procedures performed, neobladder remained well shaped during the whole follow up period proving the anatomical tolerability of this technique. Similar results have been presented by Thoeny et al [17], who also reported on the morphology and function of the upper tract and concurred on the safety of the use of an ileal segment for neobladder. In Fig. 1

Fig. 1: CT pyelography at 3 months.

Fig. 2: CT pyelography at 6 months

and 2 are presented the anatomy of the neobladder and of the upper tract at 3 and 6 months respectively. Apart the metastasis found in the two patients that died there were no any other anomalies found at CT scans.
Besides preservation of correct anatomical shape, good function is of paramount importance for a neobladder. Good function refers to adequate voiding and storage characteristics without compromising upper urinary tract safety either by high pressure urination, obstruction (eg ureteroileal), backflow of urine, stone formation or other causes. In our series urodynamic evaluation showed that neobladder capacity increased over time but remained well below 700cc which is consider by others (18) a threshold with prognostic significance of clinically important residual (>100cc). Also end-filling pressure decreased over time (23±4 vs 20±1 vs 15±1 cm H_2O), together with Qmax (19±5 vs 16±1 vs 13±4 ml/sec). These findings might differ from others [1,4,6,8,9,19-21] and might imply a "relaxation" of the neobladder. Yet, Qmax of 13±4 ml/sec is a good flow and the fact that residual remained stable and well below 100cc (69±9 ml at the end of the follow up) proves that VIP is a highly functional neobladder. The intrinsic contractions during the follow up period remained stable, while others (19) report an increase of the intrinsic contractions. They attributed these contractions to a population of Cajal cells based on the myenteric plexus of the ileum with significant contribution to gastrointestinal mobility. They are divided in two populations (ICC-MP and ICC-DMP) and their number although decreased or even disappeared (ICC-DMP) post detubularization, might remain scarce but active (ICC-MP) or even increase [22-24]. Intrinsic contraction if are big in magnitude might lead to inadequate voiding or incontinence.
In our series continence rates were high during daytime and stable with more than 87% of the patients remaining continent during the 3 years of follow up. Similarly very good outcome regarding nighttime continence was noted with more than 75% continence rates for the whole 3 years. Although direct comparison between studies regarding "continence" might not be accurate with the most obvious reason being the definition of continence itself used in each study, our results are similar to the ones reported by others [1,2,6,8,9,12] and offer a very good pattern of urination.
QoL in general is not significantly affected. Others [25-27] have already mentioned that QoL is not significantly compromised following radical cystectomy and urinary diversion. Additionally, it has not yet proven that continent diversion, although it has significant advantages in everyday life, offers higher quality of life compare to an ileal conduit [26,27]. In our series patients with VIP technique have good quality of life already six months postoperatively and this good outcome remains stable for at least 3 years. This finding can be considered as the clinical proof that the results presented for the VIP technique are translated to a quality of life of high levels.

Conclusions

VIP technique for bladder substitution after radical cystectomy is a technique with favorable results: it mimics the normal bladder anatomy and offers good function with preservation of the upper tract. Moreover QOL did not change proving its efficacy in everyday activities. Is a relatively easy technique with no additional complications and can be offered to all patients after radical cystectomy.

Author Contribution

Kostakopoulos N: Data collection and management, Data analysis;
Protogerou V: Protocol/project development, Data analysis, Manuscript writing/editing;
Varkarakis I: Protocol/project development;
Skolarikos A: Protocol/project development, Manuscript editing;
Papatsoris A: Protocol/project development;
Troupis T: Protocol/project development;
Piagou M: Protocol/project development;
Deliveliotis Ch: Protocol/project development.

Riassunto

Viene presentato uno studio completo riguardante complicazioni, immagini, risultati funzionali e clinici, e qualità di vita di una serie di 95 pazienti affetti da neoplasia transizionale localizzata (T2N0M0), trattati con VIP. Il follow up è stato eseguito ad 1, 3, 6, 12, 18, 24 e 36 mesi, con valutazione clinica ed ecografica. A 6, 12 e 36 mesi è stata eseguita una pielografia con TAC ed una valutazione urodinamica, ed è stato usato un questionario di rilevamento della funzionalità soggettiva della vescica ed il questionario EORTC QLQ C-30 di valutazione della qualità di vita. Le complicanze postoperatorie solo stati: ileo in 2 pazienti (2.1% - Grado IIIb di Clavien), un decesso postoperatorio (1.0% - Grado V di Clavien) ed un arresto cardiaco recuperato (1.0% - Grado IVa di Clavien). Le complicanze postoperatorie sono state: laparocele in 4 pazienti (4.21% - Gradi I di Clavien) e idronefrosi in 5 pazienti (5.26% - Grado IIIb di Clavien) in rapport a stenosi uretero-neovescica. In un paziente si è verificata ritenzione urinaria per stenosi cervicale della neovescica (1.0% - Grado IIIb di Clavien) ed in un paziente una fistola tra ileo e neovescica (1.0% - Grado IIIb di Clavien). Durante il follow up vi sono stati due decessi tardivi per causa oncologica (2.1%).
Dal punto di vista urodinamico si è assistito all'accrescimento della capacità della neovescica, della pressione a fine riempimento e decrement del Qmax mentre il residuo urinario ed il numero delle contrazioni intrinseche sono rimasti stabili. Continenza e qualità di vita sono state elevate e stabili durante l'intero follow up.
La tecnica della VIP per sostituzione vescicale è relativamente semplice con basso tasso di complicazioni, buoni risultati funzionali con rispetto della qualità di vita dei pazienti.

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