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The I pouch ileal neobladder: Oncological and functional outcomes

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1. Introduction

1.1 Epidemiology:

As urothelial cancer is a cancer of the environment and age, the incidence and prevalence rates increase with age and associated with environmental toxins[1].

According to the American Cancer Society statistics, there were 68,810 total cases diagnosed with bladder cancer (51,230 men and 17.580 women) accounting for 7% of all cancers[1]. By contrast in Europe 104,400 incident cases were diagnosed in 2006, (82,800 in men and 21,600 in women) which represents 6.6 % and 2.1 % of all cancer cases for men and women, respectively[2]. In men, bladder cancer is the fourth most common cancer and accounts for 4.1% of total cancer deaths in men and 1.8% of total cancer deaths in women[2].

There is a geographic difference in the incidence around the world. The highest rates are reported in Southern and Eastern Europe, North Africa, the Middle East, and North America whereas the lowest are reported in Asia and underdeveloped areas of Africa[2]. In 2002 bladder cancer was the 9th most common cancer worldwide and the 13th most common cause of death worldwide[3]. The histologic cell type of bladder cancer varies also geographically. In North America and Europe, 95% to 97% of all cases are urothelial cell carcinoma; by contrast in Africa 60% to 90% are urothelial and 10% to 40% are squamous cell cancer cases. Egypt has the highest rate of squamous cell carcinoma due to the endemic infections with Schistosoma species. The mortality rate in Egypt is 3 times higher than in Europe and 8 times greater than in North America possibly due to higher tumour aggressiveness of squamous cell carcinoma that is highly prevalent in Egypt[3].

1.2 Diagnosis and Staging:

1.2.1 Diagniosis:

EAU guidelines recommended doing cystoscopy with biopsy for urological diagnosis of invasive bladder cancer, Imaging only if staging will make a difference to the selection of treatment options and local staging for patients considered suitable for radical treatment either magnetic resonance imaging with fast dynamic contrast enhancement or multidetector-row CT with contrast enhancement.

For patients with confirmed muscle-invasive bladder cancer multidetector-row CT of the chest, abdomen and pelvis, including multidetector-row urography for complete examination of the upper urinary tracts are recommended. Lesser alternatives (e.g. if multidetector-row CT is unavailable) are excretory urography and a chest X-ray[4].

1.2.2 Staging:

TNM classification of urinary bladder cancer is described in table (1)

T - Primary tumour			
	TX		Primary tumour cannot be assessed
	T0		No evidence of primary tumour
	Ta		Non-invasive papillary carcinoma
	Tis		Carcinoma in situ: ‘flat tumour’
	T1		Tumour invades subepithelial connective tissue
	T2		Tumour invades muscle
		T2a	Tumour invades superficial muscle (inner half)
		T2b	Tumour invades deep muscle (outer half)
	T3		Tumour invades perivesical tissue
		T3a	Microscopically
		T3b	Macroscopically (extravesical mass)
	T4		Tumour invades any of the following: prostate, uterus, vagina, pelvic wall, abdominal wall
		T4a	Tumour invades prostate, uterus or vagina
		T4b	Tumour invades pelvic wall or abdominal wall
N - Lymph nodes			
	NX		Regional lymph nodes cannot be assessed
	N0		No regional lymph node metastasis
	N1		Metastasis in a single lymph node in the true pelvis (hypogastric, obturator, external iliac or presacral)
	N2		Metastasis in multiple lymph nodes in the true

			pelvis (hypogastric, obturator, external iliac or presacral)
	N3		Metastasis in common iliac lymph node(s)
M - Distant metastasis			
	M0		No distant metastasis
	M1		Distant metastasis

Table (1) TNM classification of urinary bladder cancer[5]

WHO grading

The WHO grading (1998) for bladder cancer is shown in table (2)

Grade 1	moderately differentiated
Grade 2	well differentiated
Grade 3	poorly differentiated

Table (2) The WHO grading(1998) for bladder cancer [6]

1.3 *Radical cystectomy*:

1.3.1 Indications:

Indications of radical cystectomy in bladder cancer patients include[7] T2-T4a, N0 M0 BC as well as all T1 patients if failure of intravesical therapy, recurrences after bladder sparing treatments, non-urothelial carcinomas, high risk non-muscle-invasive BC (i.e. patients with multiple tumours, high grade tumours, associated CIS)

1.3.2 Technique:

Radical cystectomy includes the removal of the tumour bearing bladder and surrounding perivesical soft tissue, adjacent distal ureters as well as prostate, and seminal vesicles in men and the ovaries, uterus/cervix, and anterior vaginal wall in women[8]. It also includes the retrieval of bilateral pelvic lymph nodes the extent of which has not been clearly defined so far[9]. Although removal of bladder and lymph nodes are the integral parts of the procedure there is a big controversy about the radicality of the surgical approach. Chang et al recommended to spare the internal female organs because involvement of the uterus, cervix, and ovaries was found to

be uncommon[10]. Furthermore preservation of the vagina and uterus provides functional better support for the neobladder and the pelvic floor[11].

A standard lymphadenectomy in bladder cancer patients involves the removal of all nodal tissue cranially up to the cross of the common iliac bifurcation with the ureter being the medial border, laterally the genitofemoral nerves and caudally the lymph node of Cloquet[12]. An extended lymphadenectomy includes all lymph nodes in the region of the aortic bifurcation and common iliac vessels medially to the crossing ureters and including the internal iliac, presacral, obturator fossa and external iliac nodes[9,13] .

Roth et al used single-photon emission computed tomography (SPECT) combined with computed tomography (CT) plus intraoperative gamma and found that lymphadenectomy limited to the ventral portion of the external iliac vessels and obturator fossa removed only about 50% of all primary lymphatic landing sites, whereas extended lymphadenectomy along the major pelvic vessels, including the internal iliac, external iliac, obturator, and common iliac region up to the uretero-iliac crossing, removed about 90% of them[14].

Since many studies have not found a minimum number of lymph nodes to be removed for accurate staging and therapeutic value in bladder cancer and interindividual differences in the number of lymph nodes , it seems reasonable to concentrate on the anatomical extent of lymphadenectomy[15]. Koppie et al found no evidence for a minimum number of LNs sufficient for optimizing bladder cancer outcomes when a limited or extended pelvic LN dissection wass performed during RC, but the probability of survival continued to rise as the number of LNs removed increased[16].

Similarly Capitanio and colleagues indicated that removing 25 LNs might represent the lowest threshold for the extent of lymphadenectomy at RC[17] .

In an attempt to preserve potency some authors reported satisfactory results reaching 79 % potency rates without compromising oncological outcomes[18]. Rozet and his colleges considered that prostate sparing RC to be a good option in selected patients with improved continence and potency rates and comparable oncological outcomes for radical cystoprostatectomy after long term follow up of sixty months[19]. However recent studies have shown that even a potency sparing approach results in 7.4% risk of incidental prostate cancer in the apex[20].

Standard RC is done by open surgery. Laparoscopic cystectomy and pelvic lymphadenectomy (with or without robotic assistance), with extracorporeal construction of urinary diversion, is an option for surgical treatment in experienced hands[7].

1.3.3 Complications:

Today, radical cystectomy is a procedure with an acceptable rate of perioperative morbidity and mortality. Improvements in surgical technique and anaesthesia as well as increased quality of perioperative care in recent years have resulted in reduced morbidity and shorter hospital stay[21]. The frequency of complications after RC varies in literature reaching up to 64% of cases[22] .

1.3.3.1 Classification:

Early and late

Early complications occur in a short, well-defined interval of 90 days after surgery whereas complications occurring later than 90 days are defined as being late. Long-term complications may develop decades later. For example a colorectal cancer may develop in patients with ureterosigmoidostoy 10 years postoperatively[23].

Primary and Secondary

Primary complications are those directly attributable to the cystectomy, including digestive system complications, accidental punctures or lacerations, postoperative fistulas, hematomas, seromas, and nonhealing surgical wounds.

Secondary complications are defined as those that occur distantly from the surgical field, in an organ system other than the urinary tract (such as cardiac, respiratory, urinary, vascular, and postoperative infectious complications) and that could occur with most types of surgery[23].

1.3.3.2 Grading of Complications:

A recent evaluation revealed that the majority of series reporting RC morbidity did not use a formal complication reporting system, nor utilize grading systems other than to categorize complications as ‘major’ or ‘minor’. In addition many series did not account for comorbidities, and define complications which made comparison of series impossible. Thus standardised methods for reporting data on surgical complications or morbidity after RC are urgently needed[24].

The Clavien system for classifying surgical complications that was originally developed in 1992[25] and modified by Dindo et al in 2004[26] represents nowadays the standard for reporting surgical complications[27].

The Clavien system (Table 3)classifies the severity of a complication, by the level of intervention required to deal with it[25].

Although this system is less suitable for the reporting of long-term, it has been used with increasing frequency since 2008 in urological community duo to its standardized and well validated structure[28].

Grade	Definition
Grade I	Any deviation from normal course after surgery with no need for pharmacological, surgical, endoscopic, and radiological interventions.Allowed therapeutic regimens includes: antiemetics, antipyretics, analgesia, diuretics, electrolytes, physiotherapy. Examples include ileus. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than allowed for grade I complications Total parenteral nutrition and blood transfusion also included
Grade III	Requiring surgical, endoscopic or radiological intervention
IIIa	Intervention not under general anaesthesia. Example radiologically guided aspiration of fluid
IIIb	Intervention under general anaesthesia.Return to theatre due to control bleeding or other complications
Grade IV	Life-threatening complication requiring intensive care management
IVa	Single organ dysfunction (including dialysis).
IVb	Multi-organ dysfunction.
Grade V	Death of a patient.

Table (3) The Clavien system for classification of surgical complications[26].

1.3.3.3 Risk factors for complications:

Two large studies have evaluated risk factors associated with complication after RC. The first study by Shabsigh et al included 1,142 patients performed by well trained urologists in the same centre

Univariate analysis identified gender, prior pelvic radiotherapy, estimated blood loss, number of packed red blood cells or fibrin patches used, and American Society of Anesthesiologists (ASA) score as significant predictors of any grade of complication. After using multivariate analysis, only gender, ASA score and type of urinary diversion were significant predictors, while prior pelvic radiotherapy and age trended towards significance[22].

Another study conducted by Hautmann et al. reported complication rate of 1,000 neobladder procedures at a tertiary academic referral center. Their univariate analysis showed that the incidence and severity of complications correlated significantly with age, tumor stage, ASA score and preoperative comorbidity[23].

1.3.4 Oncological outcomes after cystectomy:

1.3.4.1 Pelvic recurrence:

Pelvic recurrence of transitional cell carcinoma after RC is relatively infrequent but when it develops, the prognosis is poor[23]. In a large series of 1054 patients treated with radical cystectomy, the local recurrence rate was 7% after a median follow-up of 10 yr. Local recurrence rate was slightly higher in patients with nonorgan-confined node-negative disease and node-positive disease compared with organ-confined node-negative disease (13%, 13%, and 6%, respectively)[29].Therefore, the role of orthotopic bladder replacement in patients undergoing cystectomy for locally advanced or node positive bladder cancer is unclear. In these patients, there is a risk that local recurrence might cause mechanical or functional interference with the reservoir[23]. Most recurrences manifest during the first 24 months, and many are concentrated within 6 to 18 months after surgery[30].

There is no difference in the recurrence rate between patients undergoing orthotopic diversion and those undergoing heterotopic diversion[31].

1.3.4.2 Distant metastasis

Distant recurrence is noted in approximately 50% of patients treated with cystectomy, and most often (80% to 90%), this occurs within 24 months. Risk factors that increase the probability of distant recurrence are nodal status and pathologic

tumour stage. The most common sites of recurrence are the lungs, liver, and bones[30].

1.3.4.3 Upper tract recurrence:

Upper tract recurrence rates range between 2% to 9% in different cystectomy series and generally occurs 24 to 40 months after surgery. Risk factors that are associated with upper tract recurrence are patients with carcinoma in situ, urethral involvement and ureteral involvement[31].

Suspicion of an upper tract recurrence in neobladder patients not clearly visible on radiographic examinations or small superficial tumours amenable to endourologic treatment usually are a dilemma in the urological field. Access to the upper urinary tract for diagnostic and therapeutic purposes is usually not easy in neobladder patients because of many factors like an antireflux valve mechanism, a long afferent ileal segment, difficulties in localizing the ureteral neo-orifice(s) implanted end-to-side according to Nesbit, and/or ureteral kinking at the reimplanation site[9,32].

The development of smaller and flexible ureteroscopes has led to an increase use of retrograde endoscopy both for treatment as well as surveillance of upper urinary tract tumours[33].

1.3.4.4 Secondary urethral tumours:

The incidence of urethral recurrence after radical cystectomy in men ranges from 0% to 18%, with a meta-analysis in 2002 reporting an incidence of 8.1%[9,32].Urethral recurrence after cystectomy seems to be dependent on type of urinary diversion and time interval[34].Freeman and his colleges found that urethral recurrence was 5% in orthotopic neo-bladder patients versus 24% in the blind-ending urethra after heterotopic urinary diversion. Risk factors that are significantly associated with urethral recuurence after RC are prostatic involvement of urothelial carcinoma, tumour multifocality, and type of urinary diversion[35]. Early symptoms of secondary urethral tumors may include hematuria (microscopic or gross) and changes in urinary stream. However the detection of asymptomatic UR is associated with significantly lower stage disease and improved patient survival[35].

Urethral recurrence occurs in 3% to 15% of women and is associated with tumor at the bladder neck[30]. However, because 50% of women with bladder neck and/or anterior vaginal wall involvement do not demonstrate tumor within the urethra, these patients can still be eligible for orthotopic diversion if urethral margins at frozen section are negative[9,36].

1.4 Survival after cystectomy:

Construction of nomograms for survival prediction had been performed by several groups. The principle advantage of this approach is that it provides a survival probability for individual cases with different predictive indices accuracy reaching up to 83.4%. This enables the clinicians to make the best decision in patient counselling, selecting the optimal adjuvant therapy and follow up schedule[37-41]. Outcome is best characterized by disease-specific survival versus overall survival, which underestimates the impact of treatment in patients with favourable tumor and nodal stage.

In a large multicentre study a higher final pathological tumor stage, lymphovascular invasion, lymph node metastasis, adjuvant radiotherapy and adjuvant systemic chemotherapy were independently associated with recurrence free survival. Increasing patient age, higher final pathological tumor stage, lymphovascular invasion, lymph node metastasis and adjuvant radiotherapy were independently associated with cancer specific survival[42].

The largest single centre study up to date showed that the 5- and 10-yr RFS for patients with organ-confined, lymph node–negative tumours were 85% and 82%, respectively, and OS at 5 and 10 yr was 78% and 56%, respectively. The 5- and 10-yr RFS and OS for patients with non–organ-confined, lymph node– negative tumours was 58% and 55%, respectively, and 47% and 27%, respectively[29].

Some evidence suggests that elevated preoperative serum CRP and presence of thrombocytosis are associated with decreased survival outcomes[9,43,44].

1.5 Quality of life after cystectomy:

Several questionnaires have been validated for assessing health related quality of life (HRQoL) in patients with bladder cancer, including FACT (Functional Assessment of Cancer Therapy)-G[45], EORTC QLQ-C30[46], EORTC QLQ-BLM (muscle invasive bladder cancer module)[47], SF (Short Form)-36[48] and recently the

bladder cancer index (BCI) questionnaire specifically designed and validated for bladder cancer patients[49].

After careful analysis of all the QoL studies, it becomes evident there is a lack of good data evaluating QoL in patients with OBS versus other diversions. Most QoL studies used inappropriate questionnaires. Although some are validated, they were not designed to evaluate specific urologic aspects but rather QoL of patients during chemotherapy[36].

Published evidence does not support an advantage of one type of reconstruction over the others with regard to QOL. An important proposed reason for this is that patients are subjected preoperatively to method-to-patient matching, and thus are prepared for disadvantages associated with different methods[34]. Randomized prospective trials using well-validated disease-specific health-related QoL outcome instruments are warranted to render definitive conclusions regarding QoL measures with different type of diversions[36].

1.6 Urinary diversion:

1.6.1 Types

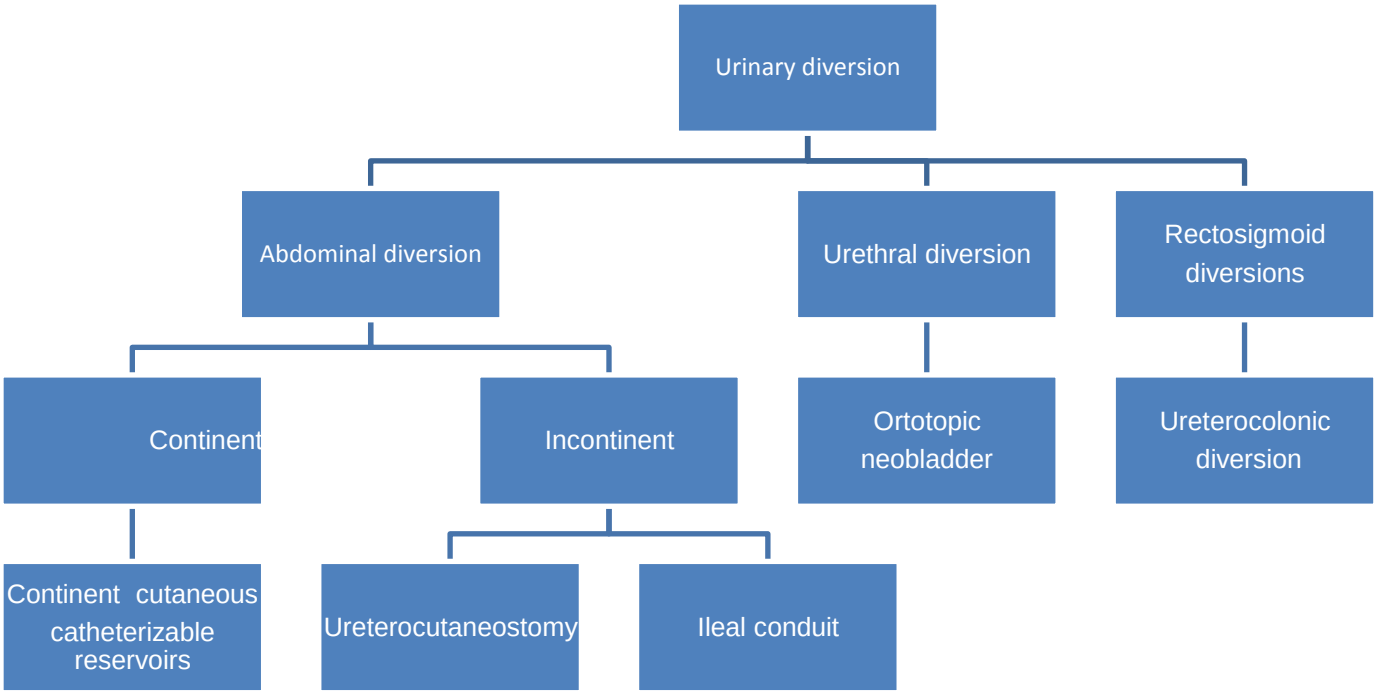

Fig. (1) Types of urinary diversion

The choice of the urinary diversion after cystectomy depends on many factors both cancer-related (tumour stage) and patient-related factors. The latter includes the patient's general health and social circumstances, baseline renal function, presence of a functional urethra, manual dexterity, and previous treatments including pelvic radiation, prostate surgery, or bowel resection. The ability of the patient to manage the diversion can only be judged by personal experience while talking to him, taking into account his social status and his capability to eventually perform a clean intermittent catheterization[50,51].

The current status of distribution of various urinary diversions after cystectomy for bladder cancer reflects a report of Hautmann and coworkers evaluating > 7000 patients: neobladder, 47%; conduit, 33%; anal diversion, 10%; continent cutaneous diversion, 8%; and incontinent cutaneous diversion, 2% (fig.1)[34].

1.6.1.1 Ureterocutaneostomy

Technically either one ureter to which the other shorter one is attached end-to-side is connected to the skin (transuretero-ureterocutaneostomy) or both ureters are directly anastomosed to the skin[52].

Ureteral diversion to the abdominal wall is the simplest form of cutaneous diversion. It is considered as a safe procedure. It is therefore preferred in older and compromised patients, who need a supravesical shunt instead of ileal coduit as this type of urinary conversion requires a long intestinal segment to create a pouch as well as longer operative time. Therefore, this invasive method is limited to patients in good general condition with long life expectancy[52,53].

Earlier, a stomal stenosis rate of about 50% in cutaneous ureterostomy has limited its application restricting to patients with hydroureter[54].

Claman and his colleagues suggested that one could succeed in transplanting even a normal-calibre ureter to skin, as long as basic principles of preservation of blood supply and avoidance of angulation and tension are respected[55].

After development of many techniques and improvement of surgical dissections recent data in a retrospective comparison with short or median follow-up of 16 months showed that the diversion-related complication rate was considerably lower for ureterocutaneostomy compared to an ileal or colon conduit[56].

1.6.1.2 Ileal conduit

This is the most common form of diversion used in conjunction with cystectomy. A 15- to 20-cm-long distal ileal segment is isolated, and ureters are implanted in the proximal end. The stoma is usually below and to the right of the umbilicus[34].

A colonic conduit is most often used when high-dose irradiation has been given previously. When an ileal conduit is used in such patients, the risk of complications is very high[34].

Up to 48% of the patients undergoing ileal coduit develop early complications including urinary tract infections, pyelonephritis, uretero-ileal leakage and stenosis[51].

An increase in complications was seen with increased follow-up after a minimum of 5 years .the rate of complications increased from 45% at 5 years to 94% in those surviving longer than 15 years[57].

1.6.1.3 Continent cutaneous urinary diversion

A high-pressure detubularised ileal reservoir can be used as a continent cutaneous urinary diversion wherein urine is emptied at intervals by clean intermittent self-catheterization. Gastric, ileocecal and sigma pouches have also been described. Ureters have to be placed in an antireflux manner[58].

Different antireflux techniques can be used, namely 1. Appendiceal techniques, pseudoappendiceal tubes fashioned from ileum or right colon, and the ileocecal valve placation 2. Tapered and/or imprecated terminal ileum and ileocecal valve. 3. Use of the intussuscepted nipple valve or, more recently, the flap valve, which avoids the need for intussusception. 4. Provision of a hydraulic valve[50,59].

The cutaneous ileocecal pouch is a safe and proven technique for continent urinary diversion in patients in whom orthotopic pouch urinary diversion is not feasible. Continence mechanisms have acceptable complication rates and offer highly satisfactory continence rate with daytime and night time continence approaching 93%[60].

Mansson and colleagues found no difference in overall quality of life in men undergoing continent cutaneous diversion when compared with orthotopic neobladder[61].

1.6.1.4 Ureterocolonic diversion

The oldest and most common form was primarily a refluxive and later an antirefluxive connection of ureters into the intact rectosigmoideum (uretero [recto]sigmoidostomy). Most of the indications for this procedure have become obsolete due to a high incidence of upper urinary tract infections and the long-term risk of developing colon cancer There is also generally a 10- to 20-year delay before the cancer becomes manifest. Because cancer incidence is significant in patients with ureterosigmoidostomies, patients should do routine colonoscopies on a scheduled periodic basis[50,62,63]. Bissada et al found that renal function remained stable in 92% of their patients[64] .

Bowel frequency and urge incontinence were additional side-effects of this type of urinary diversion. However, it may be possible to circumvent the above-mentioned problems by interposing a segment of ileum between ureters and rectum or sigmoid in order to augment capacity and to avoid a direct interaction between urothelium, colonic mucosa, together with faeces and urine[65].

1.6.1.5 Orthotopic neobladder

The first extensive clinical experience with orthotopic substitution was reported by Camey and Le Duc in 1979 in male bladder cancer patients[66].

An orthotopic bladder substitution to the urethra is now commonly used both in men and women. Contemporary reports document the safety and long-term reliability of this procedure. In several large centres, this has become the diversion of choice for most patients undergoing cystectomy[34,67,68].

The terminal ileum is the gastrointestinal segment most often used for bladder substitution and there is less experience with ascending colon, including caecum, and the sigmoid[34,69].

The emptying of the reservoir anastomosed to the urethra requires abdominal straining, intestinal peristalsis and sphincter relaxation. Currently, it is not possible to recommend a particular type of urinary diversion. However, most institutions will prefer ileal orthotopic neobladders and ileal conduits based on clinical experience[70]. The only oncologic contraindication to orthotopic diversion is the presence of tumor on the urethral margin, which can be safely checked intraoperatively[51].

1.6.2 The ileal orthotopic neobladder

1.6.2.1 Contraindications

The absolute oncological contraindication is a positive frozen section or positive soft tissue margins other absolute non- oncological contraindications include Urinary stress incontinence, a damaged rhabdosphincter or incompetent urethra, Impaired renal function (serum creatinine > 150– 200 lmol/l) and severe intestinal diseases (e.g., Crohn's disease, short bowel syndrome).

Relative contraindications include tumour infiltration of the distal prostatic urethra in men or bladder neck in females, impaired intellectual capacity, dexterity and mobility[9].

1.6.2.2 Basic principles

The two important properties for continent urinary reservoir construction are to store urine at a low pressure without significant high-pressure reflux[71].

Detubularized and folded segments provide these characteristics using shorter length of bowel needed compared with non detubularized segments[72]. Ileum is the preferred bowel segment because it has less contractility and better compliance compared with colon and cecum.

Based on Laplace's law, the pressure of a reservoir is defined as P = T x 2 D / R, in which P is pressure, T is the mural tension, D is the thickness of the wall, and R is the radius. Thus, intraluminal pressure is inversely correlated to the radius of a spherical reservoir. A tubular segment with its small radius will reach already-high kidney-deteriorating intraluminal pressures at low volumes. A spherical reservoir, however, will maintain the largest capacity with the lowest pressure due to a larger radius[73].

Other advantages of the spherical reservoir are a maximum volume to surface area ratio, with maximal volume and minimal reabsortive surface area; detubularization and cross-folding of the bowel segment render coordinated contractions impossible and minimize the development of high pressure peaks; with maximum radius, wall tension is also maximal and thus a sensation of filling is more likely[74].

As a result of mucosal atrophy over the long term, ileal segments have less reabsorption of urinary wastes and electrolytes compared with colonic segments[75].

1.6.2.3 Uretero ileal anastamoses

a) Surgical principles

Although many techniques have been described to make the various types of ureterointestinal anastomosis, certain principles are applied to all the anastomosis regardless of type.

- As much ureter as needed should be mobilized so that there should be no redundancy or tension on the anastomosis.
- Mobilization should not strip the ureter of its periadventitial tissue because it is in this tissue that the ureter's blood supply courses.
- The ureter should be cleaned of its adventitial tissue only for 2 to 3 mm at its most distal portion where the ureter-intestinal mucosa anastomosis is to be performed.
- The ureterointestinal anastomosis should be performed with fine absorbable sutures, which are placed so that a watertight mucosa-to-mucosa apposition is constructed.
- The intestine should be brought to the ureter and not vice versa (i.e., the ureter should not be extensively mobilized so that it can be brought into the wound to the bowel lying on the anterior abdominal wall)[50].
- In a randomized study stented versus non stented anastomosis showed that complications were reduced and allowed for early recovery of bowel activity [76].

b) *Refluxing or anti reflux anastamoses*

Because studies comparing refluxing versus non refluxing urinary diversion have generally been limited by short follow-up, patient selection bias, retrospective design, or relatively small patient numbers there are still controversies regarding the necessity of antireflux mechanism in low-pressure orthotopic substitutes[77].

Arguments of doing reflux anastamoses are that the orthotopic bladder substitutes are low-pressure reservoirs, as detubularized bowel segments are incapable of coordinated contraction and pressure generation so reflux can not occur as pressure inside the reservoir is lower than that of the ureters, another factor is that urine in the bladder substitute is sterile. In addition, the afferent tubular segment itself has certain dynamic antirefluxive properties due to coordinated peristalsis[74]. Finally many antireflux methods are technically challenging and are potentially accompanied

by considerable complications such as ureteroenteric stricture with subsequent upper-tract deterioration.

Arguments for the incorporation of an antireflux mechanism in orthotopic neobladders include the high percentage of bacteria in ileal reservoirs and an antirefluxive protection of the upper urinary tract in the native bladder[69].

Currently, there is no compelling evidence of whether a refluxing isoperistaltic ileal segment or a non refluxing (eg, subserosal, nipple) ureteral implantation will provide better long-term protection of the upper urinary tract[34].

c) *Techniques of ureteroileal anastamoses*

- *Refluxing techniques*

I. Bricker Anastamoses:

This is a refluxing end-to-side ureter–small bowel anastomosis that is simple to be performed and has a low complication rate[78]. The adventitia of the ureter is sutured to the serosa of the bowel. Sutures approximate the ureter to the full thickness of the mucosa and serosa.

II. Wallace Technique:

Refluxing anastomosis in which the end of the intestine is sutured to the end of the ureter[79].

Both the Bricker and the Wallace anastomosis provide acceptably low stricture rates. However the walllace technique shows better outcomes[80].

- *Non Refluxing techniques*

I. Le Duc Technique:

The ureter implanted and introduced into the lumen of the reservoir via a transmural non refluxing channel and left unfixed intraluminally[81].

II. Split-Nipple Technique:

The ureter is spatulated approximately 1 cm and folded back to form a split-cuff nipple. The corners are sewn to each other except for a small gap proximally to prevent constriction. The ureter is then placed into the bowel such that it protrudes through the mucosa[82].

III. Kock ileal valve:

The Kock nipple antireflux technique uses an ileal segment as an antireflux mechanism to create an intussuscepted ileal valve[83]. The ureters then implanted directly in the ileal segment

IV. Serous-lined extramural tunnel:

Placing the ureters directly into serous-lined extramural tunnels[84] provides reflux protection in W shaped reservoirs.

1.6.2.4 Techniques for ileal orthotopic substitution

- *Orthotopic substitution on a U-shaped and cross-folded reservoir (“Goodwin principle”)*

I. Camey II

A total of 65 cm of ileum is isolated. The ileum is placed in a transverse U orientation,the ureteroileal anastomosis is performed by a Le Duc technique[85].

II. Studer ileal neobladder

This technique uses a 60- to 65-cm segment of terminal ileum. The distal 40- to 45-cm segment is opened antimesenterically and serves as the reservoir, whereas the proximal 20- to 25-cm ileal segment remains intact and serves for ureteral implantation and prevention of reflux by isoperistaltic waves. The proximal end of the afferent intact segment is closed, and after spatulating and stenting the ureters, the ureterointestinal anastomosis is performed separately for both ureters with an end-to-side technique at the proximal end[86].

III. The orthotopic Kock ileal pouch

Two approximately 22-cm distal ileal segments are placed in U-form to create the pouch whereas an approximately 17-cm ileal segment is used to create an intussuscepted 5- to 7-cm ileal valve. The ureters are then implanted directly in the intussuscepted ileal segment at the proximal end[83].

IV. The T-pouch ileal neobladder

It has the same spherical configuration as the Kock ileal neobladder; the only difference is the use of an afferent ileal segment instead of an intussuscepted ileal valve as an antireflux system (‘‘T-limb’’)[87].

V. The Padovana ileal neobladder

A 40-cm segment of terminal ileum is used. The proximal loop is folded in a reverse S-shape and the ureters are implanted via two serous-lined intestinal troughs[88].

VI. The I pouch

This type uses 40 cm from the terminal ileum. The ureters are joined together using the modified Wallace technique and then reimplanted in a subserosal tunnel at the upper end of the pouch[89]. It is called I pouch because the ureters are implanted in a vertical manner in the contrary to T pouch[69]. This type will be discussed in details later as it is the research topic for this thesis**.**

- *W- or M-ileal reconfiguration*

I. Hautmann ileal neobladder

W-configured spherical reservoir using approximately 70 cm of distal ileum. The ureters are implanted refluxively[90].

II. W-reservoir with serous-lined extramural tunnel

A 40-cm segment of terminal ileum is used. The medial limbs are sutured together while the two lateral flaps are joined by a seromuscular running suture to create the two serous-lined intestinal troughs. The ureters are anastomosized to the intestinal mucosa. Then the tunnel is closed over the ureters forming an antireflux mechanism[84].

1.7 Objectives of the study:

1. Evaluation of the safety of this technique and its impact on the perioperative outcomes especially the complication rate according to the modified clavien system.

2. To analyze the efficacy of cystectomy and I poch ileal neobladder regarding the oncological outcomes including survival rates, recurrence and tumour stages. This will be achieved via comparing both results this technique and other ileal neobladder in literature.

3. Assessment of the functional outcome of this new technique including the quality of life through various types of questionnaires and the urodynamic characters of the I pouch (capacity, pouch pressure, postmicturition residual urine and urethral closure pressure)

2. Materials and methods

2.1 Study design:

Retrospective hospital-based clinical study (oncological and functional data). Prospective clinical study (questionnaires and urodyamic parameters)

2.2 Target population:

All patients with bladder carcinoma that underwent radical cystectomy, both genders, for urothelial and non urothelial tumour at any age who attended the department of urology, Tuebingen University hospital, starting from January 1999 until August 2011.

2.3 Sample size:

97 Patients

2.4 Inclusion criteria:

1. Bladder cancer patients that underwent cystectomy and I pouch neobladder as an orthotopic continent urinary diversion
2. Stage T 1-4a bladder cancer
3. any N stage
4. M0 or M1
5. Any tumour grade
6. American Society of Anesthesiologists [ASA] scores 1-3.
   ASA 1: Those with no serious disease.
   ASA 2: Those who may have a serious disease, but have no limitation on their activities.
   ASA 3: Those with serious disease and some limitation of their activities [91].
7. Any body mass index [BMI].

2.5 Exclusion criteria:

1. Patients underwent cystectomy with types of diversion other that I-pouch neobladder.
2. Uncontrolled coagulation disorders.

3. Patients with soft tissue margins.
4. Patients with urinary stress incontinence.
5. Impaired renal function (serum creatinine > 1.50– 2 mg/dl).
6. Patients with severely impaired liver function.
7. Patients with severe intestinal diseases (e.g., Crohn's disease).
8. Patients with impaired intellectual capacity, dexterity and mobility.
9. Patients with life expectancy lower than 5 years.
10. Untreated active urinary tract infection.
11. Azotaemia.
12. Patients who are unfit for surgery.
13. Patients who refuse the planned procedure.

2.6 Preoperative evaluation:

1. Detailed history and physical examination.
2. Estimation of body mass index.
3. Routine laboratory work-up:
    - Urine analysis and urine culture
    - Renal function tests
    - Complete blood picture
    - Bleeding and coagulation profile
    - Blood sugar level
    - Liver fuction test
    - Electrolytes evaluation
4. Imaging studies:

    a) <u>Obligatory</u>

    - Ultrasonography
    - Contrast computerized abdominal Tomography(CCT) or Magnetic Resonance Tomography (MRI)
    - Contrast computerized chest Tomography (CT)
    - Chest X ray, electrocardiography (ECG)

    b) <u>Fakultative</u>

    - A positron emission tomography computed tomography (PET/CT) in some cases with nodal invovement
    - Renal nuclear scanning when parenchymal damage is considered.

- Echocardiography

5. Evaluation of the anaesthesiological risk

According to the American Society of Anaesthesiologists (ASA) classification of physical status.

6. Consent of the patient

2.7 Operative Technique:

- All patients receive a mechanical and antibacterial bowel preparation the day before surgery.
- All patients are site-marked for a cutaneous stoma, instructed in the care of a cutaneous diversion (continent or incontinent form), and instructed in proper catheterization techniques if medical, technical or oncological factors preclude orthotopic reconstruction.
- A vertical midline incision is made extending from the pubic symphysis 2-3 cm above the umbilicus (rotating around it)
- Pelvic lymphadenectomy is done at least to the level of common iliac artery bifurcation depending on the stage of bladder cancer
- Radical cystectomy is done with the trial to preserve the neurovascular bundle and the external urethral sphincter if oncologically feasible.
- Good haemostasis
- Construction of the I pouch ileal neobladder

Technique of I pouch ileal neobladder construction

- The 2 ureters are spatulated and joined together using the modified Wallace technique using 5-0 vicryl and stented using a Single J stent (Fig. 2).

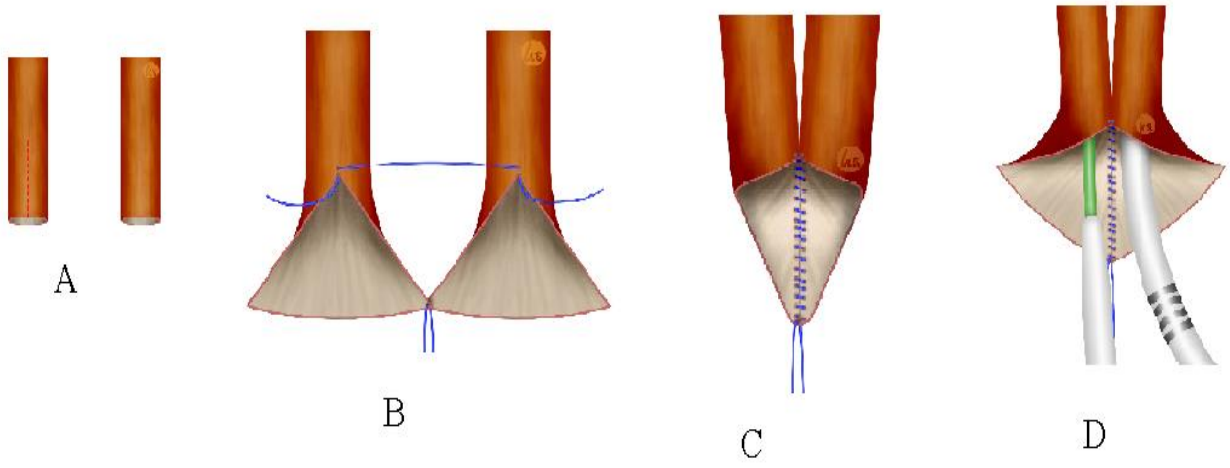

Fig. (2) *A*. ends of the 2 ureters *B.* The 2 ureters spatulated *C.* and joined together according to modified Wallace technique *D.* The 2 ureters are stented with single J stents

- An ileal segment 40 cm long is isolated 15-20 cm proximal to the ileocaecal valve and bowel continuity restored with a running suture (3-0 PDS).
- A Goodwin pouch is formed with a U-shaped ileal plate (length of each limb: 20 cm) that is cross-folded (Fig. 3).

Fig. (3) The U-shaped ileal plate

- 8 cm of the paramesentric borders are sutured together to make the posterior wall of the future ureteric trough (Fig. 4).

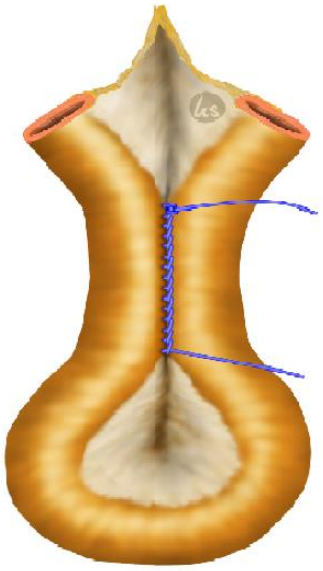

Fig (4) preparation of the ureteric trough

- Both ileal loops are opened by scissors at the antimesentric borders 2 cm from the beginning of the loops to the site of future ureter implantation (8 cm) to go medially to be paramesentric at this point and then complete the opening at the antimesentric border (Fig. 5).

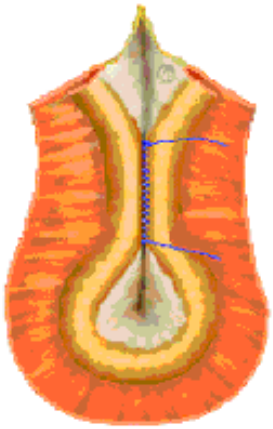

Fig. (5) Opening of the ileal loop

- The ureters are sutured with the intestinal mucosa using a 5-0 running suture. Then the seromuscular layers of both loops are sutured together over the ureters thereby completing the trough (Fig.6).

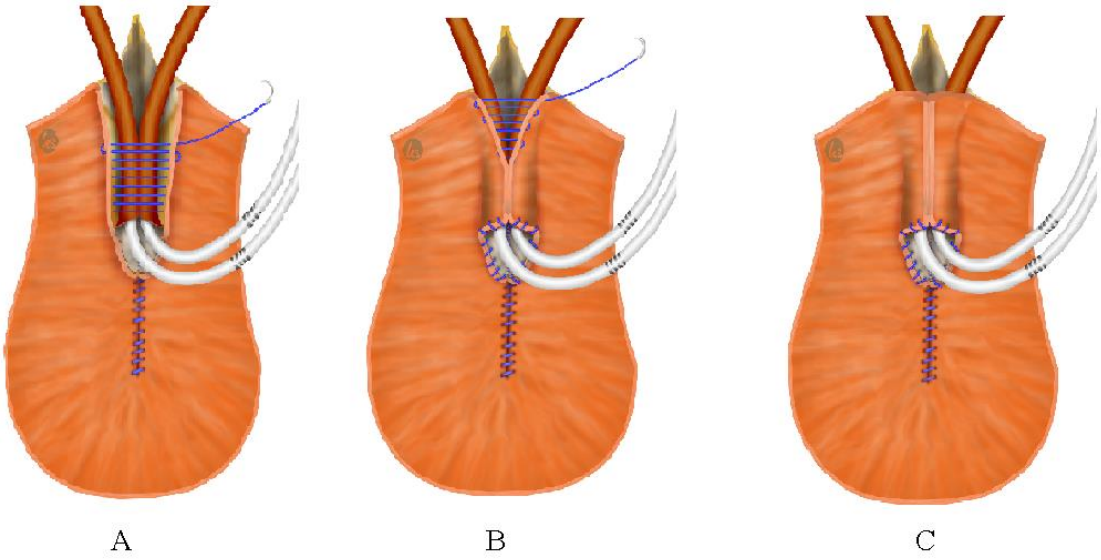

Fig. (6) *A.* Placement of the 2 ureters in the though *B.* and anastomosized the 2 ureters with the intestinal mucosa *C.* Closure of the seromuscular layer of the loops over the ureters completing the trough.

- The upper and lower edges of the intestinal loops are joined together forming the configuration of the pouch according to Godwin's principle. The single J stents are externalized through two separate openings in the mesentery. Then the edges are sutured together leaving the dependent part of the pouch to be connected to the urethra in males while in female all the edges of the pouch are closed and an opening at the most lower dependant part of the pouch is opened and then sutured to the urethra (Fig. 7).

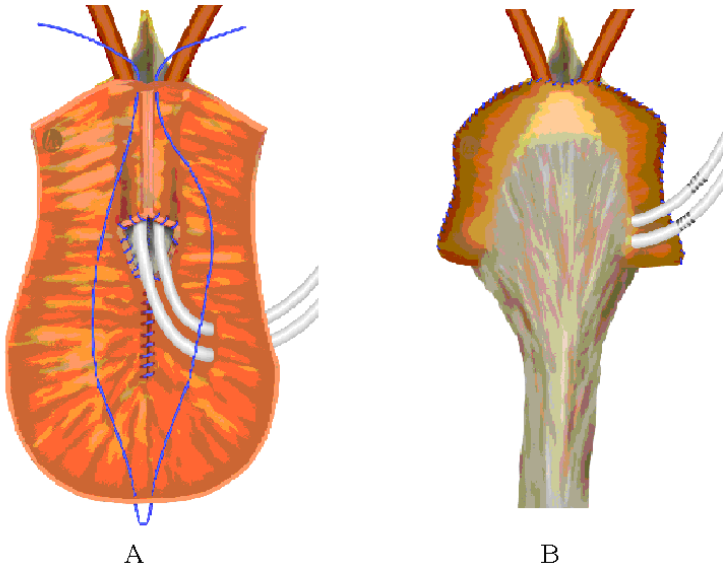

Fig.(7) *A.* upper and lower edges of the intestinal loops are joined together *B.* stents are externalized through two separate openings in the mesentery

2.8 Postoperative Follow up:

2.8.1 Perioperative outcomes:

Hospital charts and physician records were reviewed to determine clinical outcomes

1. Evaluation of complications according to the new modified Clavien system[25].
2. Estimation of postoperative renal function
3. Collection of demographic characters of the patients (age, sex, number)

2.8.2 Oncological outcomes:

The histological assessment was performed in one pathology department and was conducted according to the new 2009 TNM classification

1. Reporting the oncological outcome from pathological reports including tumour stage, tumour type, tumour location, tumour grade, nodal stage, nodal number, presence of metastasis, lymphovascular invasion urethral and ureteric margins.
2. Reporting the recurrence free survival by evaluation of the follow up CT and MR
3. Reporting the overall survival by collecting the data from the local tumour registry.

2.8.3 Functinal outcomes

2.8.3.1 Questionnaire:

Contacting living patients for sending the follow up questionnaire

4 types of questionnaire were used

EORTC QLQ-C30 and QLQ- BLM

The QLQ-C30 version 3 is a cancer-specific, self-administered, structured questionnaire designed for use in clinical trials[92].

It contains 30 questions (items) measuring 3 general items Global health status score, functional score and symptom score.

For the global health score the scale ranges from 1 to 7 where 1 is very poor and 7 is excellent. The higher the score the better the health status.

For the global quality of life score the scale ranges from 1 to 7 where 1 is very poor and 7 is excellent. The higher the score the better the health status.

The QLQ-BLM30 comprises 30 questions assessing disease symptoms, side-effects of treatment with special consideration to urinary symptoms, incontinence and sexual function and some specific psychosocial issues of importance to patients with muscle invasive bladder cancer.

Items 1 to 7 address urinary symptoms and problems. The higher score the worse the symptoms. (Range 7-28).

SF-36

The SF-36 version 1 is a multi-purpose, short-form health survey with only 36 questions[48]. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index. The 8 items are physical functioning, role of limitation due to physical health, role of limitation due to emotional problems, energy/fatigue, emotional well being, social functioning, pain and general health.
The higher the score, the better the function (Range 0-100)

The Gastrointestinal Quality of Life Index (GIQLI)

The five questions from the Gastrointestinal Quality of Life Index concerning bowel habits are used[93] and the patients were asked to answer them retrospectively before doing the cystectomy (as far as they remember) and 2 weeks after the operation (as far as they remember) in order to determine the changes of bowel habits that occurred as a result from the operation. This is of special importance in the study to know whether the bowel habits of the patients who received an I pouch (with the use of only 40 cm segment of terminal ileum in contrast of most other neobladders) had been affected.

Special type of questionnaire

12 questions were developed by an institutional protocol in an attempt to complete the items needed to be evaluated which are considered to be missed by the other questionnaires.

2.3.8.2 Urodynamics:

Contacting living patients for doing the follow up urodynamics (10 patients accepted).

After placement of a 6F transurethral dual channel catheter and a 14F rectal balloon catheter, the neobladder was filled at a rate of 20 mL/min with saline solution at room temperature. Uroflowmetry, cystometry, and urethral pressure profilometry were performed. The evaluated parameters were the neobladder capacity, pressure at maximal capacity, urine leakage, postvoid residual urine volume, and urethral pressure profile.

2.9 Statistical analysis:

The statistical analysis was performed using jmp 10 (2012, SAS Institute Inc., Cary, NC, USA).

For univariate analysis, the Fisher's exact/Pearson chi-square test was used for nominal data and the Student's *t*-test for scaled data. All *P*-values were two-sided with $P < 0.05$ considered to indicate statistical significance. Values are given as mean, median and standard deviation for all continuous variables or as median (range) for nonparametric variables. Kaplan Meyer curves were used for the overall survival data and recurrence free survival data.

2.10 Ethical considerations:

Confidentiality:

The confidentiality of all participants admitted to this study is protected to the fullest extent possible. The study participants are not identifiable by name in any report or publication resulting from data collected in this study.

Ethical committee approval

The ethical committee of Tübingen University approved the questionnaire delivered to the patients as well as the urodynamic follow up study (Ethical approval number 063/2012BO2).

Research statement:

Ethical aspects, whether substantial or procedural, is implicated in this study. Before participants were admitted in this study, the purpose and nature of the study as well as risks were explained to them. The participants agreed that he/she understood the investigational and operative nature of this study, its inherent risks

and benefits, other treatment alternatives, his/her rights to terminate participation in this study without affecting his/her rights in having proper health care in the study site, whom to contact with questions regarding the study and that he/she is freely given an informed consent to participate in this study.

Informed consent:

The signed informed consent form is a prominent part of the participant's study records and is maintained in the same manner as other records.

3. Results

3.1 Preoperative data

3.1.1 Number of Patients

Between January 1999 until August 2011, 331 Patients underwent cystectomy and urinary diversion for bladder cancer.

Of these 331 Patients, 97 (29.3%) underwent cystectomy and I pouch ileal neobladder as urinary diversion.

3.1.2 Sex

25 females (25.8%) and 72 Male (74.2%) (Fig.8)

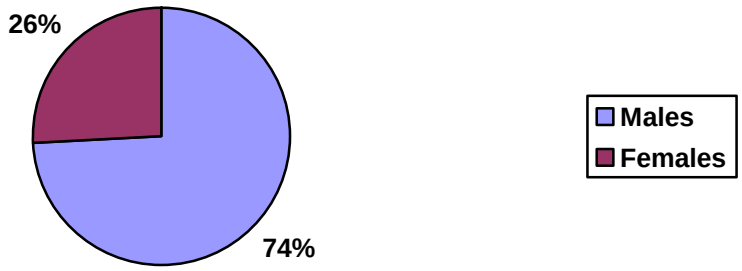

Fig. (8) shows the male: female percentage of the I pouch patients

3.1.3 Age

Median age at the time of cystectomy was 65 (42-84) years

Age groups at cystectomy are as follow (Fig.9).

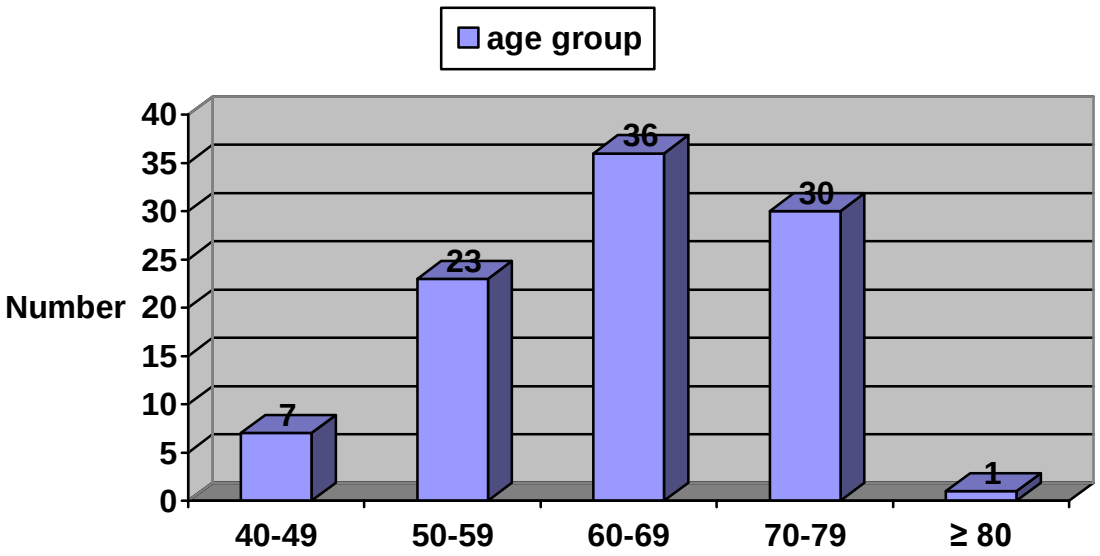

Fig. (9) shows the different age groups of the I pouch patients

3.2 Pathology

3.2.1 Tumour type

Pure urothelial bladder carcinoma was present in 91 patients, squamous cell carcinoma in 5 patients and only one patient had mixed components of urothelial and adenocarcinoma. Pure adenocarcinoma or sarcoma did not occur in this series (Fig. 10).

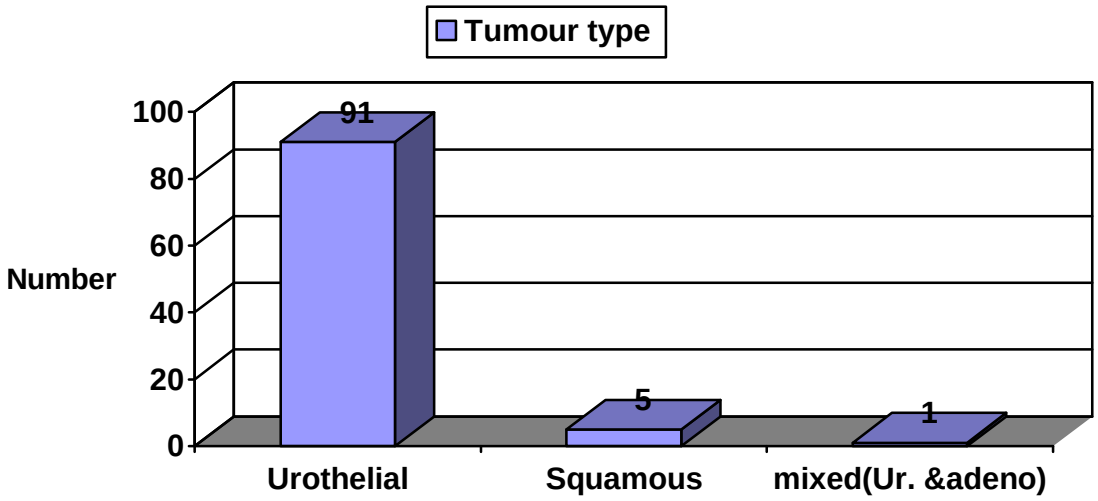

Fig.(10) shows the different types of tumour pathology in the I pouch patients

3.2.2 Tumour stage

pTa: 7 cases had non invasive papillary carcinoma

pT1: 21 cases showed infiltration to the sub epithelial tissues

pT2a: 17 cases had only superficial muscle layer invasion

pT2b: 18 cases with deep muscle invasive bladder cancer

pT3a: 15 cases had microscopic extravesical infltration

pT3b: 13 cases had macroscopic extravesical infltration

pT4a: 6 cases showed infiltration to the prostate

pT4b: no cases with pelvic or abdominal wall infltration

pTis: 30 cases had associated carcinoma in situ (Fig. 11).

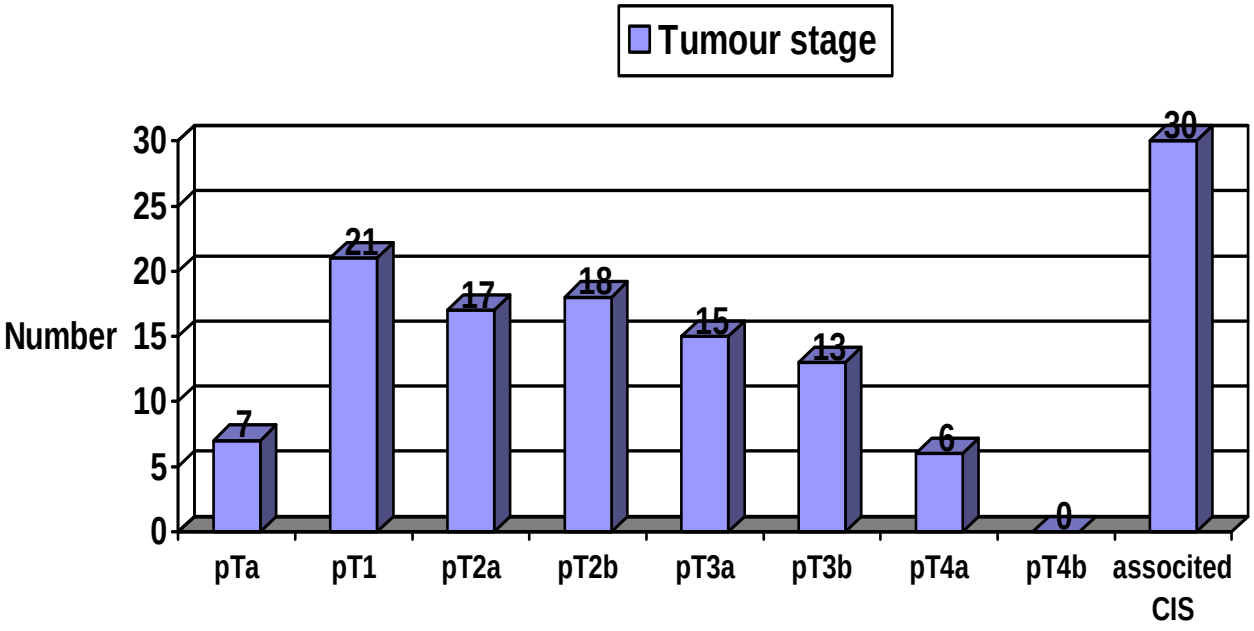

Fig. (11) shows the different tumour stages in the I pouch patients

3.2.3 Tumour grade

The tumour grades of patients underwent cystectomy and I pouch are shown in (Fig. 12).

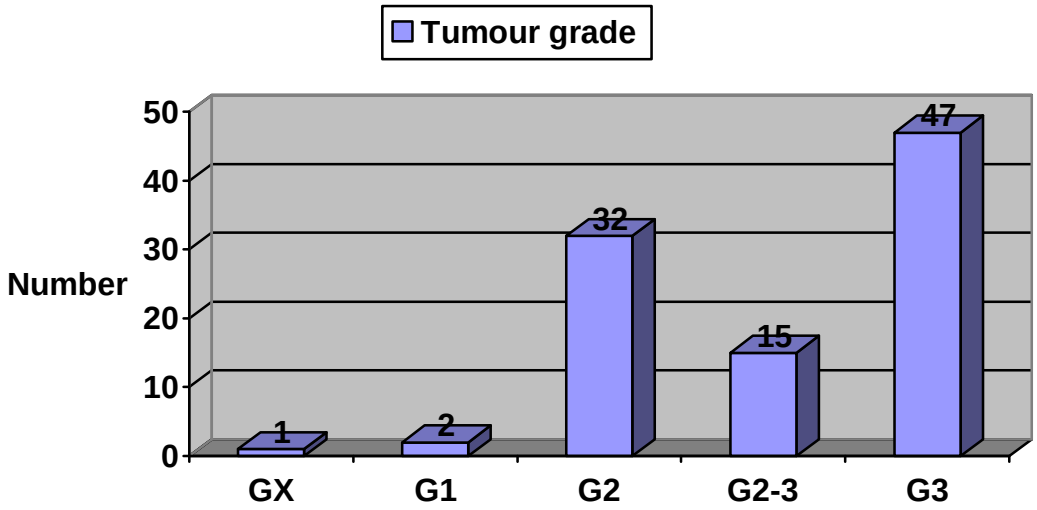

Fig. (12) shows the different tumour grades in the I pouch patients

3.2.4 Tumour site

Tumour occurred in different regions of the bladder (side walls, bladder dome, anterior wall, trigone, bladder base, bladder-neck, posterior wall, ureteric orifices and perineural) (Fig.13).

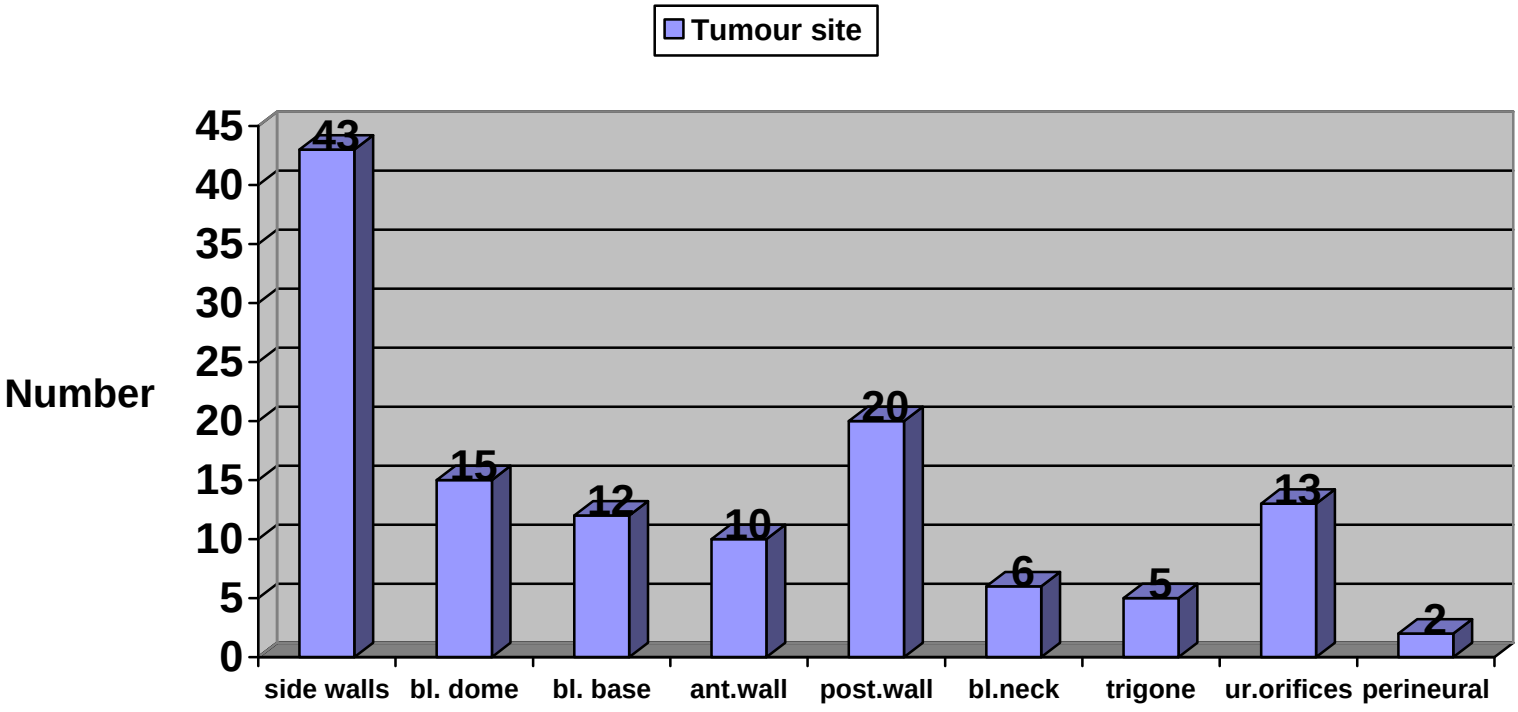

Fig. (13) shows the site of the tumor for the I pouch patients

3.2.5 Tumour multifocality

78 patients had a single tumour and 29 patients had multifocal tumour (Fig.14).

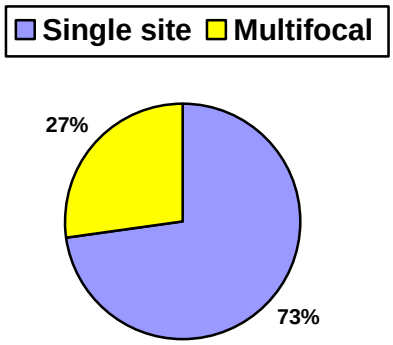

Fig. 14 shows percentage of tumor multifocality in the I pouch patients

3.2.6 Lymph nodes number

The median number of lymph nodes retrieved is 20 (0-38).

3.2.7 Node stage

The following figure showed the various node stages for all patients (Fig. 15).

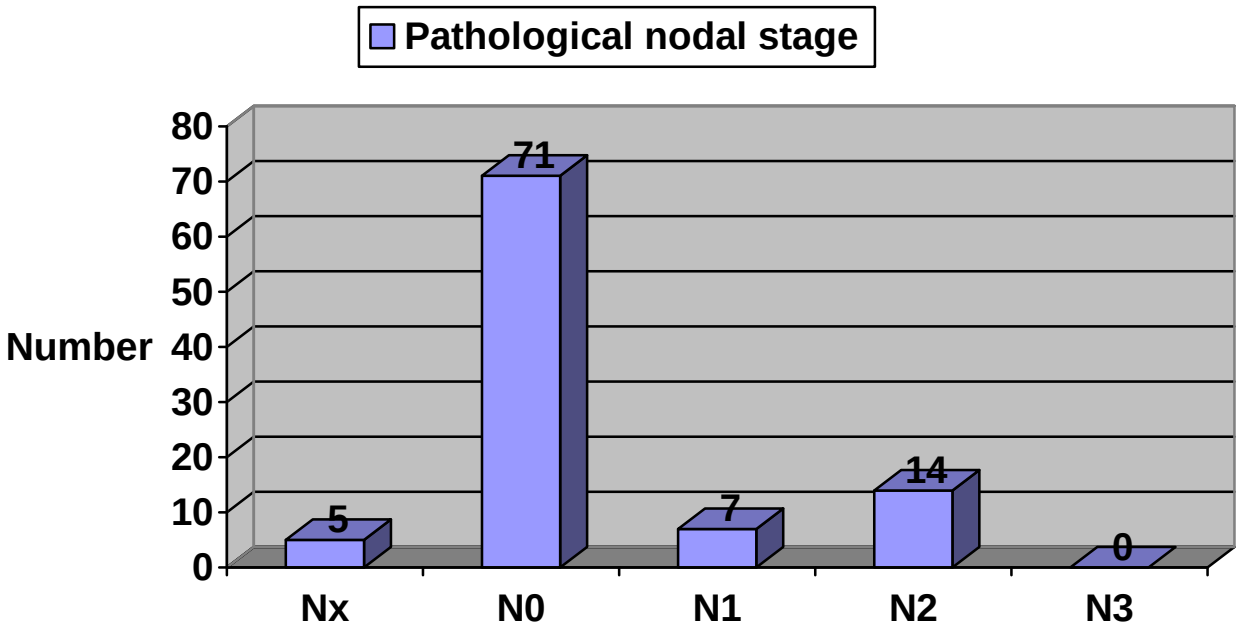

Fig.(15) shows nodal stage for the I pouch patients

3.2.8 Distant metastasis at time of cystectomy (M Stage)

Only 3 patients had distant metastases (M1) at time of cystectomy, one patient had metastases in the lung, one to the peritoneum and a neuroendocrinal metastasis (Fig. 16).

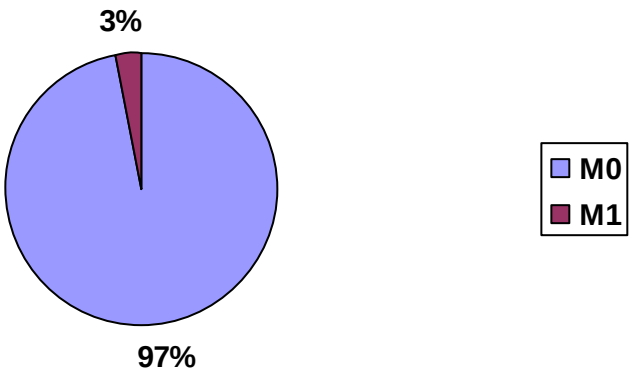

Fig.(16) shows distant metastases at time of cystectomy for the I pouch patients

3.2.9 R Stage

91 patients had no residual tumour after cystectomy (R0)

Only 6 patients had microscopic positive resection margins after cystectomy with clinical evidence of negative margin at the time of radical cystectomy.

No patients experienced R2 (macroscopic residual tumour) (Fig. 17).

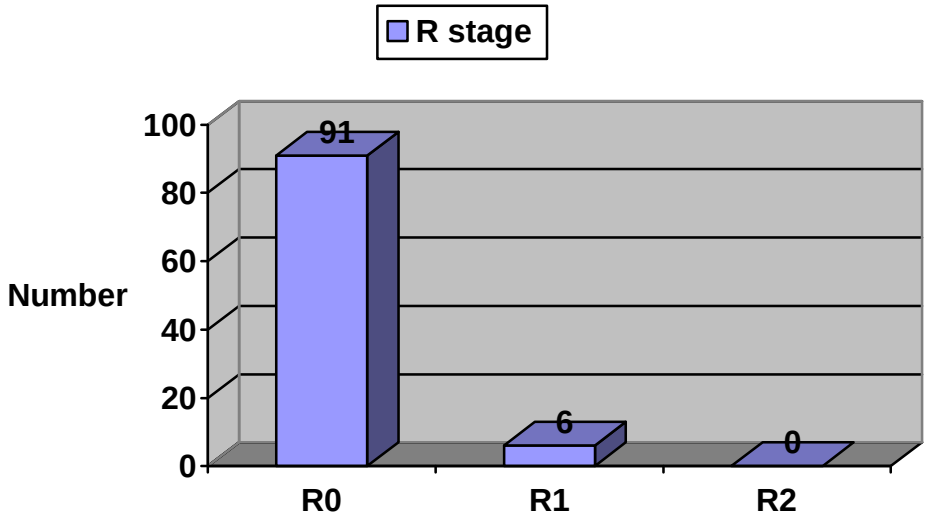

Fig.(17) shows R stage for the I pouch patients

3.2.10 L stage and V Stage

The lymphovascular invasion of the removed bladders is as following

LX: Lymphatic vessel invasion cannot be assisted in one patient

L0: No lymphatic vessel invasion in 69 patients

L1: Lymphatic vessel invasion in 27 patients

Vx: Venous invasion cannot be assessed in 2 patients

V0: No venous invasion in 87 patients

V1: Microscopic venous invasion in 8 patients

3.2.11 Urethral and ureteral margins

Only 4 patients had positive urethral margins (4.1%) in the final specimen (formalin-fixed, parafferine embedded), 3 of them were positive in frozen section. All of them are CIS.

Ureteral margins showed positive results in frozen sections in 5 patients (2 right ureter and 3 left ureter). 8 patients showed positive results in the final specimen (formalin-fixed, parafferine embedded) (3 right ureter and 5 left ureter) all of them are CIS.

3.3 Survival:

3.3.1 Recurrence free survival

Fig. 18 shows Kaplan Meyer curve for recurrence free survival. The mean time of follow up was 35 months. (Median 23.9 months, range 1.9-107.2)

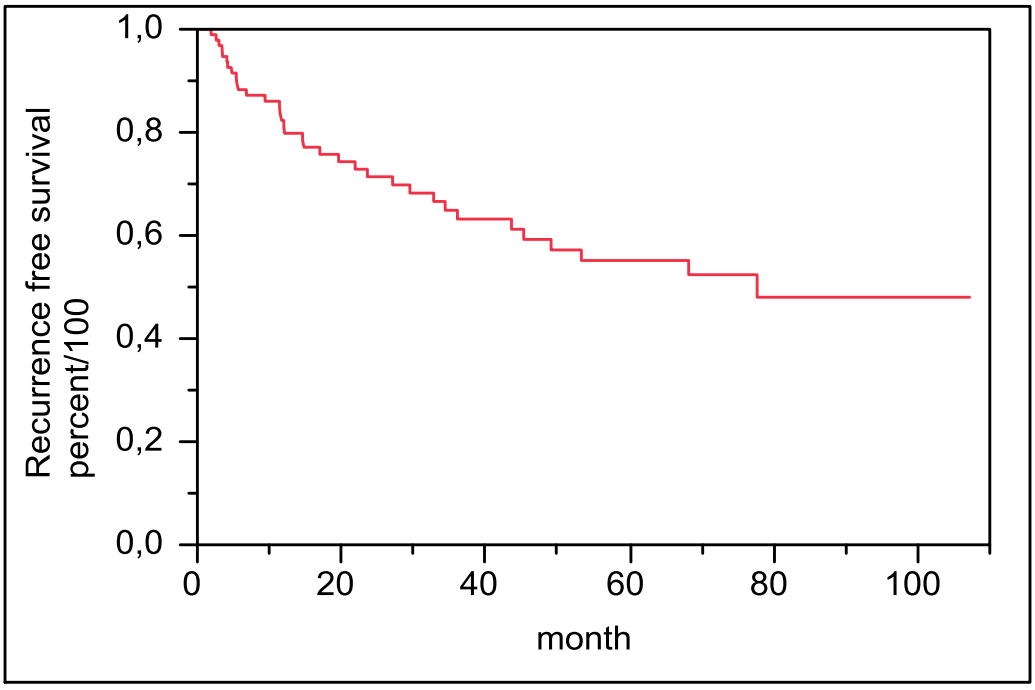

Fig. (18) shows recurrence free survival in the 97 patients with I pouch neobladder

Number of patients with recurrences at given intervals (Table 4).

Time (in months)	0	12	24	36	48	60
Number of patients died	0	18	24	29	31	33
Survival rate	100 %	79.8 %	71.4 %	63.2 %	59.2 %	55.1 %

Table (4) shows number of I pouch patients with recurrences at given intervals

Recurrence free survival for patients according to tumour and lymph node stage

The 5 years recurrence free survival for patients with organ confined tumour and negative lymph nodes (≤pT2b, N0) was 70.8 % (Fig. 19).

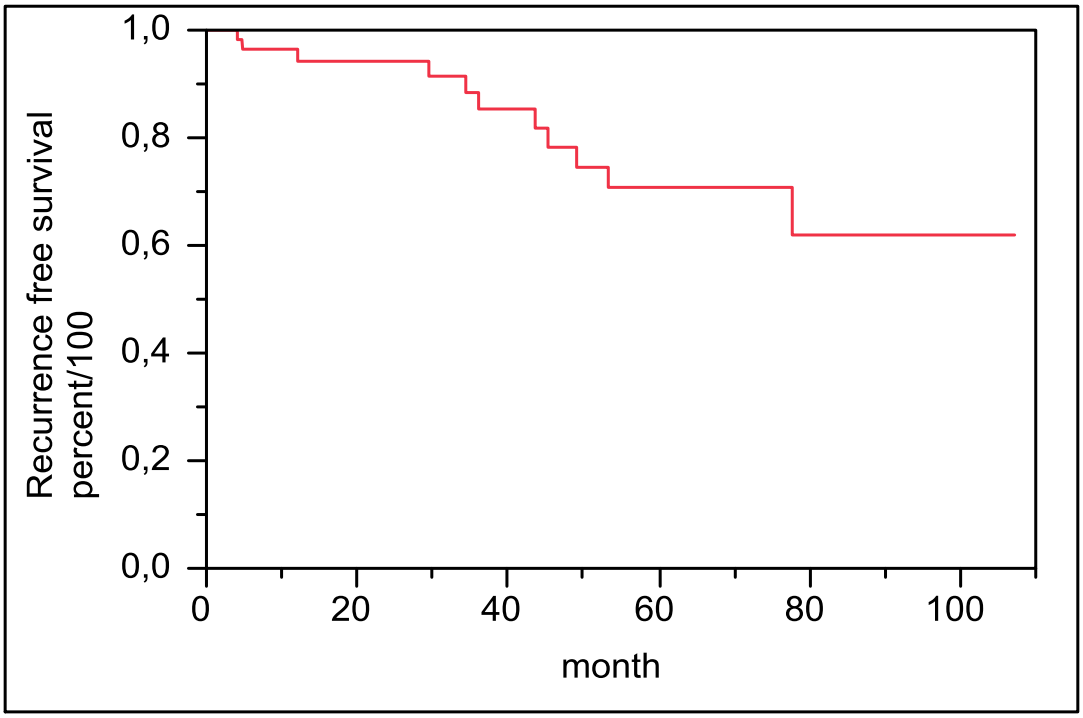

Fig. (19) shows recurrence free survival in patients with (≤pT2b, N0) (N=58)

The 5 years recurrence free survival for patients having non organ confined tumour and positive lymph nodes (≥pT3a and pN1 or pN2) was 11.7 % (Fig.20)

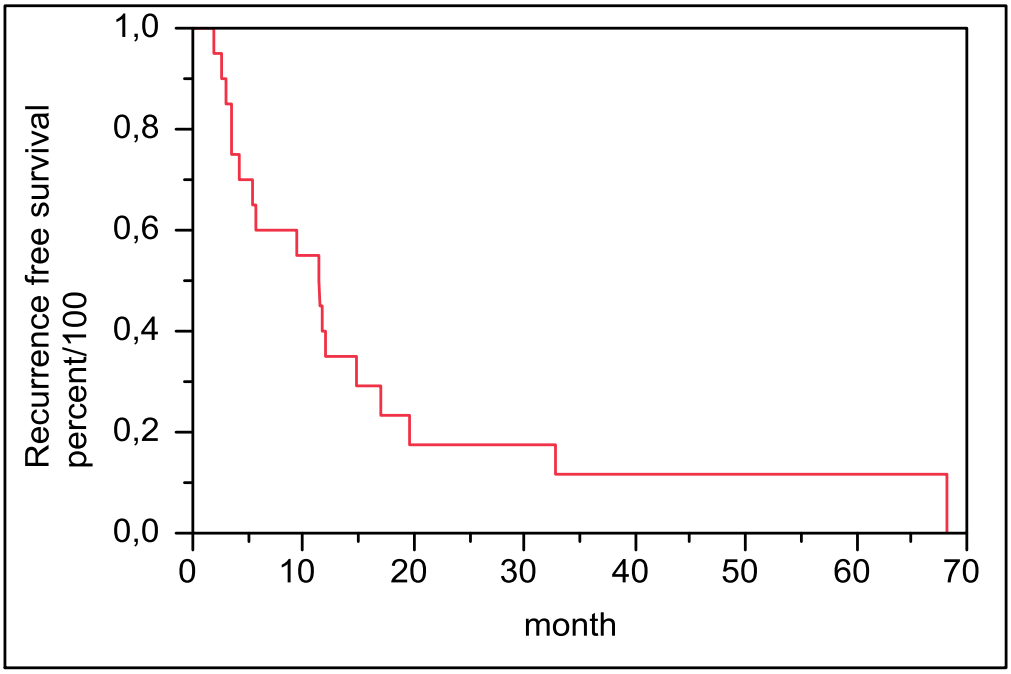

Fig. (20) shows recurrence free survival in patients with (≥pT3a and pN1 or pN2) (N=20)

3.3.2 Cancer specific survival

Fig 21 shows Kaplan Meyer curve for cancer specific survival. The median time of follow up was 40.6 months, (range 3.3-107.2)

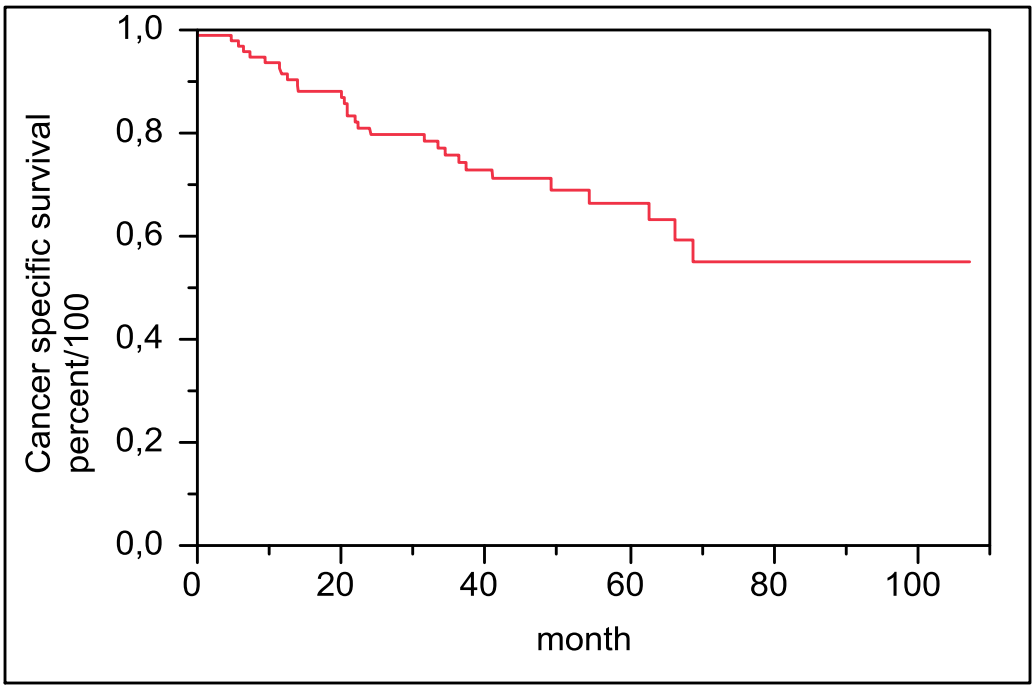

Fig. (21) shows cancer specific survival in the 97 patients with I pouch neobladder

Number of patients died due to urothelial cancer at given intervals (table 5)

Time (in months)	0	12	24	36	48	60
Number of patients died due to cancer	0	8	18	22	23	25
Survival rate	100 %	91.4%	79.7 %	74.3 %	72.8 %	67.9 %

Table (5) shows number of patients died due to cancer recurrences at given intervals

3.3.3 Overall survival

Fig 22 shows Kaplan Meyer curve for overall survival

Median time of follow up was 40.6 months, (range 3.3-107.2)

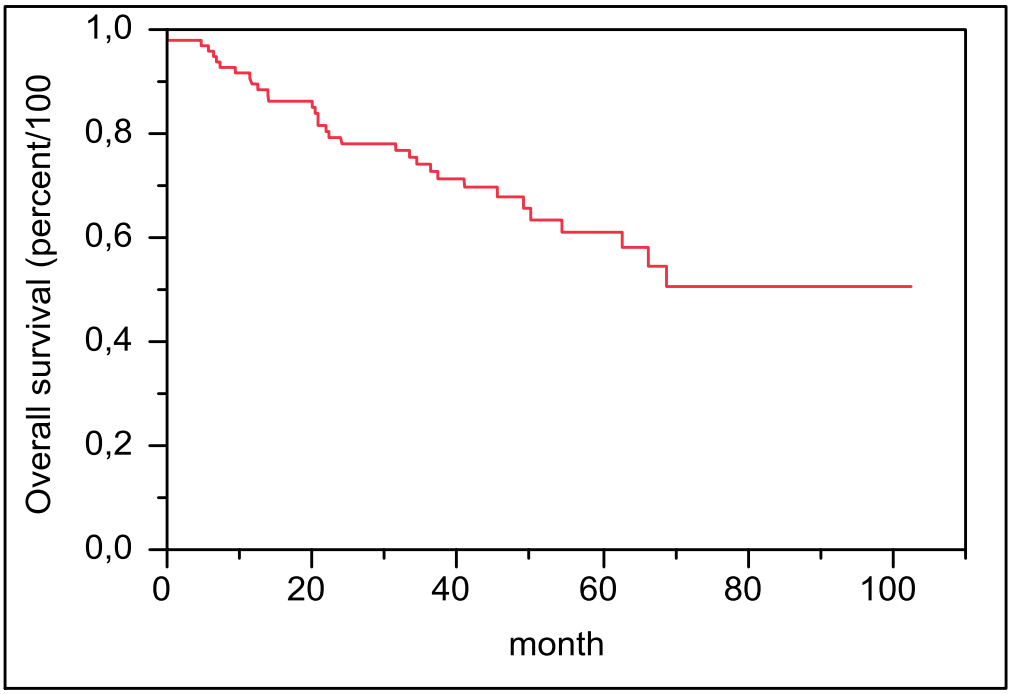

Fig. (22) shows overall survival in the 97 patients with I pouch neobladder

Number of patients died at given intervals (table 6).

Time (in months)	0	12	24	36	48	60
Number of patients died	0	8	18	22	25	28
Survival rate	100 %	91.4%	79.7 %	74.3 %	69.2 %	62.2 %

Table (6) shows number of patients died at given intervals

Over all survival for patients according to tumour stage and lymph node stage

The 5 years overall survival for patients having organ confined tumour and negative lymph nodes was only 76.4 % (Fig.23)

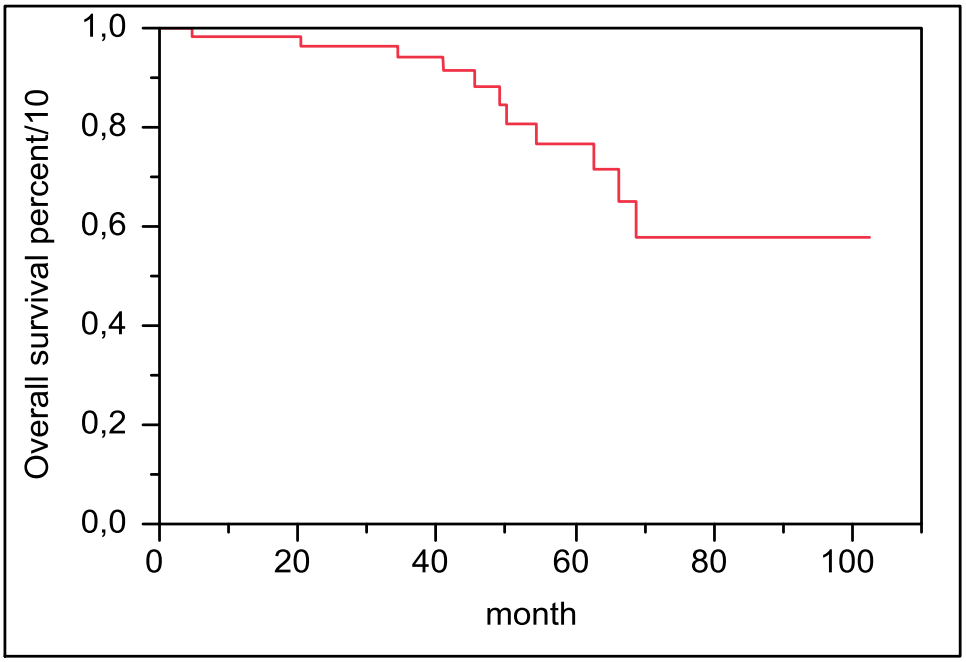

Fig. (23) shows overall survival in patients with (≤pT2b, N0) (N=58)

The 5 years overall survival for patients having non organ confined tumour and positive lymph nodes (≥pT3a and pN1 or pN2) was 11.5 % (Fig. 24).

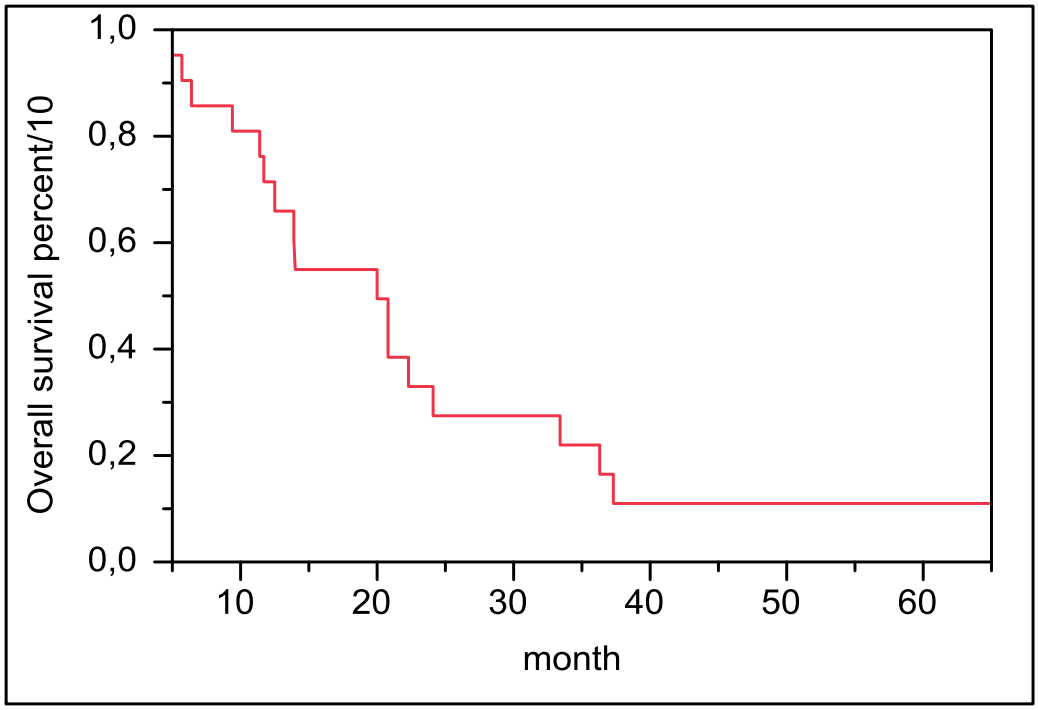

Fig. (24) shows overall survival in patients with (≥pT3a and pN1 or pN2) (N=21)

3.4 Complications:

Thirty-five (36.1%) patients had complications in the early postoperative period (30 days after operation), with addional 3 patients experienced complications in the late postoperative period (90 days after the operation) making the total complication rate 39.2%.

One complication occurred intra operatively and treated during the operation (intestinal injury → repair) which can not be accurately calculated by the modified Clavien grading. A patient experienced a non surgery related cerebral aneurism which was treated medically.

The other 37 complications (table 7) are grade I (10 patients), grade 2 (11 patients) grade IIIA (3 Patients) grade IIIB (9 Patients) IVA (2 Patients).grade IVB (one Patient) and grade V in 2 patients (Fig.25).

The cause of death was pulmonary embolism in one patient and intestinal leakage and subsequent peritonitis in the other.

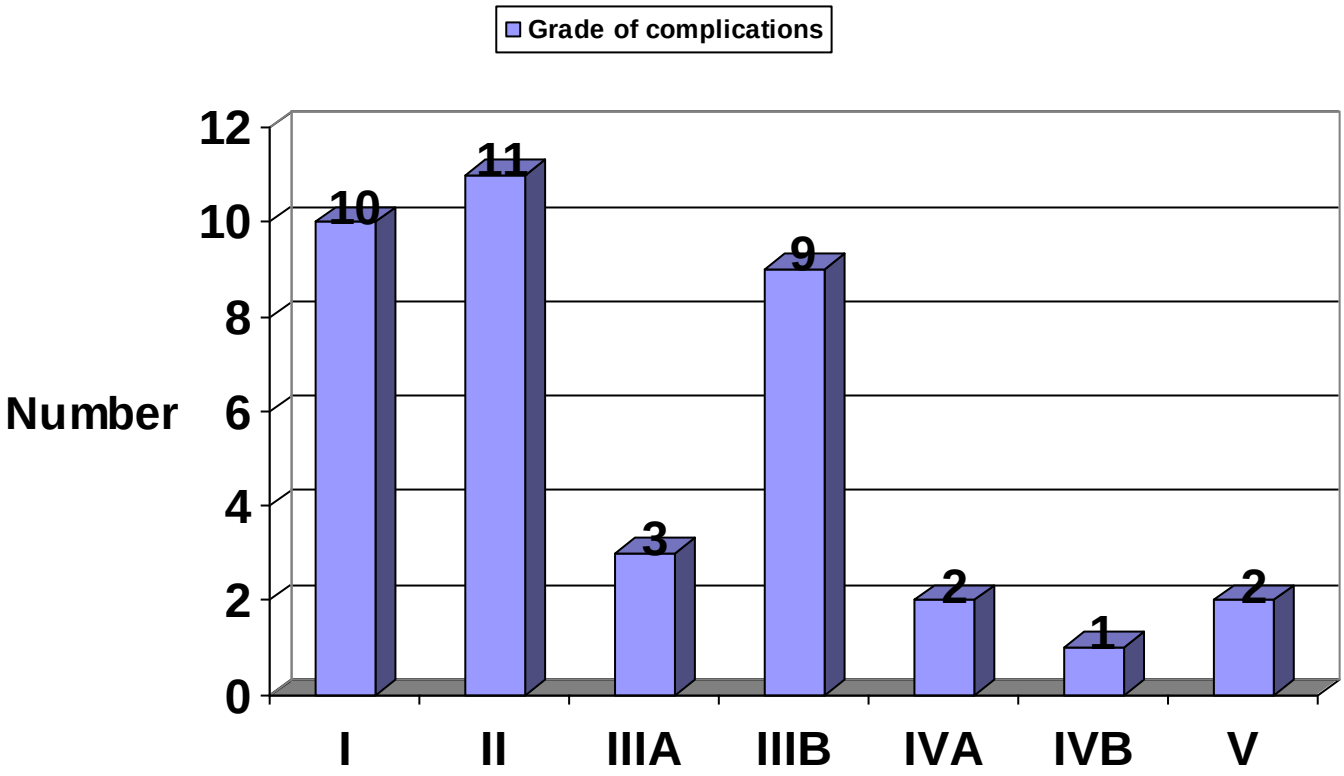

Fig. (25) Number of complications graded according to the modified Clavien system[26]

Type of complication	Number of patients	Early	Late	Grade
Fever > 38.5	4	4	0	I
Hypokaleamia	3	3	0	I
Delayed intestinal mobility	2	2	0	I
Prolonged vomiting	1	1	0	I
Blood transfusion	4	4	0	II
Paralytic ileus	3	3	0	II
Lynphocele → conservative treatment	2	2	0	II
Scrotal swelling	1	1	0	II
Wound infection	1	1	0	II
Lymphocele → percutaneous drainage	3	2	1	IIIA

Obstruction → treated endoscopicaly by antegrade JJ	4	3	1	IIIB
Intestinal obstruction → Resection - reanastamosis	2	2	0	IIIB
Rectal injury → repair	1	1	0	IIIB
Burst abdomen→ Closure	1	1	0	IIIB
umbalical hernia → Repair	1	0	1	IIIB
Hemiparesis	1	1	0	IVA
Lung emboli	1	1	0	IVA
Septic schock	1	1	0	IVB
Death	2	2	0	V
Total	38	35	3	

Table (7) shows different type of complications occurred in the postoperative period in patients with I pouch

3.5 Postoperative functional data:

3.5.1 Spontaneous voiding

93 patients of 95 patients can micturate spontaneously (97.9%) with only 2 patients requiring CIC (clean intermittent catheterization) to empty their neobladders.

3.5.2 Residual urine after micturition

The median volume of postmicturition residual urine was 0, (range: 0-200).

3.5.3 Postoperative reflux

Only one patient had direct postoperative reflux (1%) detected by postoperative voiding cystogram.

3.5.4 Postoperative hydronephrosis

16 patients developed some degree of hydronephrosis in the early postoperative period (16.5%). In 9 of those patients the hydronephrosis required no treatment and resolved spontaneously (9.3%).

The remaining 7 patients required intervention to treat the hydronephrosis. Four patients required temporary PCN and JJ, one patient had temporary JJ stent

only and only 2 patients had to undergo surgical intervention. Thus, the true ureterointestinal stenosis rate in the 97 patients was collectively 2.1 % (Fig.26).

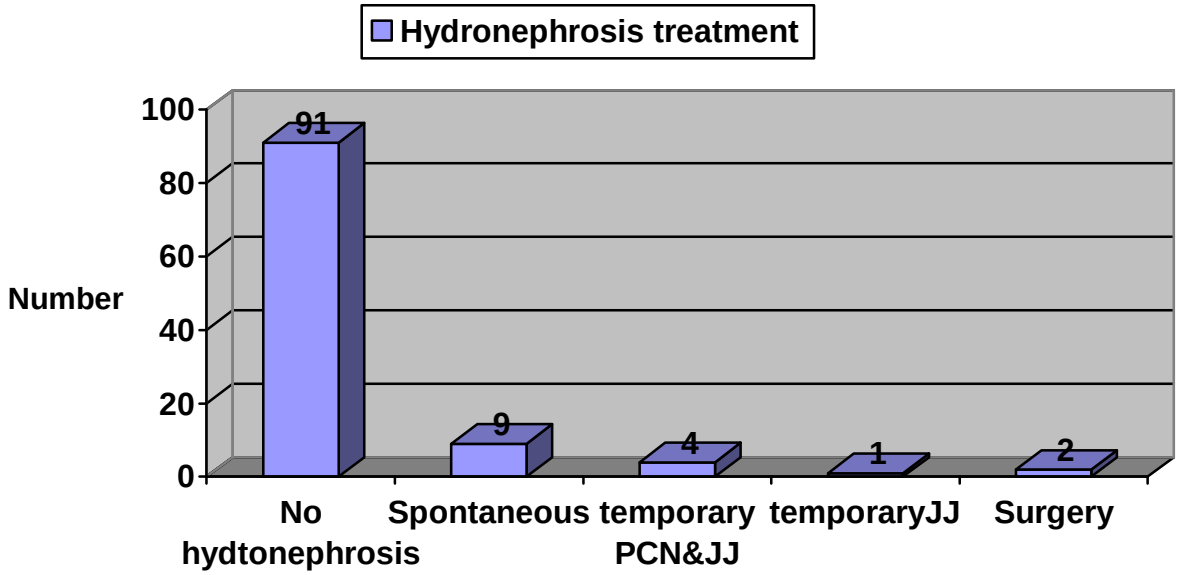

Fig. (26) shows ureterointestinal obstruction occurred in patients with I pouch and its management

3.5.6 Neobladder capacity

The mean capacity of I pouch neobladder was 235 ± 109.2 ml, (range:50-550).

3.5.7 Urinary tract infection

The median number of UTI per year was 0, (range: 0-2).

3.6 Questionnaire results:

63 patients were contacted. From those only 48 patients were reached and informed about the study and asked to answer the questionnaire. Thirty nine patients only accepted to participate.

The questionnaire were printed in German language and sent with mail to the 39 patients. Thirty three (52.4%) patients sent the full answered questionnaire back to our hospital.

The median follow up time from cystectomy date to the date of answering questionnaire was 44 month (range 9-89)

3.6.1 QLQ-C30

It consists of 30 questions that measure three big items (Global health status / QoL, Functional scales and symptoms scales).

3.6.1.1 Global health status

It has a separate question (No 29) in which the patient estimates on a scale his overall health status. The scale ranges from 1 to 7 where 1 is very poor and 7 is excellent. The higher the score the better health status.

The mean score was 75.2 ± 20.5, (Median score was 83.3; range: 16.7-100).

3.6.1.2 Quality of life

It has a separate question (No 30) in which the patient estimates on a scale his overall quality of life. The scale ranges from 1 to 7 where 1 is very poor and 7 is excellent. The higher the score the better quality of life.

The mean score was 73.2 ± 19.5, (Median score was 83.3; range 33.3-100).

3.6.2 QLQ-BLM30

It consists of 30 question evaluating different items. 6 questions (from 8 to13) were excluded from analysis because they are assessing urostomy problems and another one because it is applied only if the patient uses a catheter.

3.6.2.1 Urinary symptoms

These are 7 items describing the urinary symptoms, Each item ranges from 1 to 4 in which 1 indicates that the patient does not have any symptom and 4 indicates that the patient suffers from the symptom very much.

The urinary symptom score ranges from 0 to 100. The higher the score the worse the condition.

The mean score was 32.2 ± 20.2, (Median score was 28.6; range 0-85.7)

3.6.2.2 Sexual function

These are 8 questions for reporting sexual function and sexual problems occurring during sexual activity. Men have different questions from women. The EORTC group advised that every item should be analyzed separately. As a reason that some of the questions are not fully answered from many patients we will analyze only whether or not the patients are sexually active.

Twenty one patients (63.7%) remained sexually active after the operation while only 12 (36.3%) patients lost their sexual activity (Fig. 27).

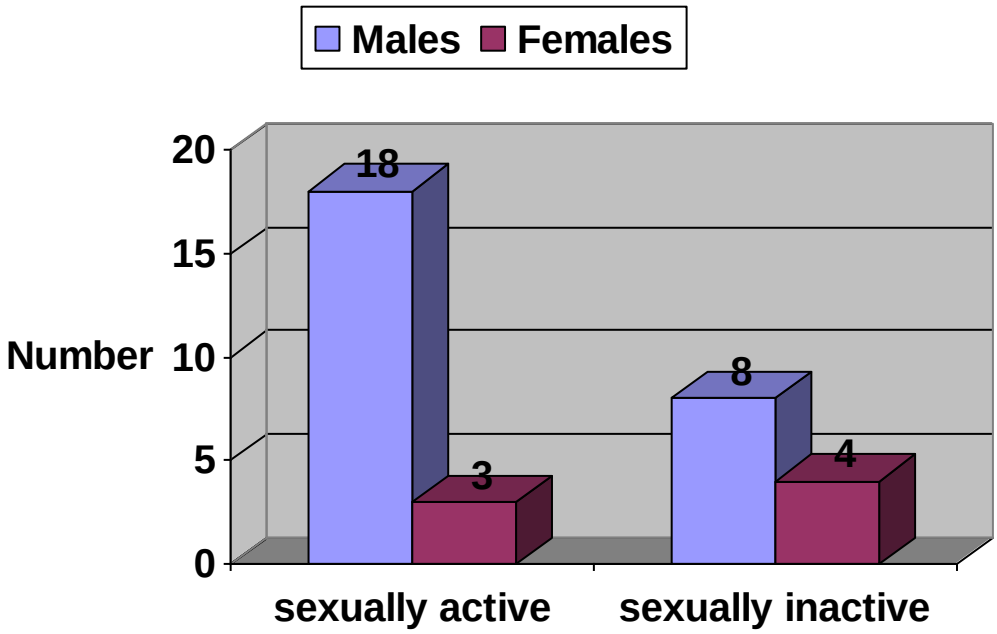

Fig (27) shows postoperative sexual function for both males and females

3.6.2.3 Other BLM-30 items

These are 8 items evaluating different parameters (future perspective, abdominal bloating and flatulence and body image). Scoring ranges from 8-32. The higher the score the worse the symptoms.

The mean score was 15 ± 4.3, (median 15; range 8-23)

3.6.3 SF- 36

Table(8) lists the different parameters of Sf-36 for the I pouch patients

The higher the score the better the quality of life regarding the evaluated item.

SF-36 Item	Mean	SD	Median	Range
SF-36 Physical functioning	78.2	25.7	85	10-100
SF-36 Role of limitation due to physical health	76.5	37.5	100	0-100

SF-36 Role of limitation due to emotional problems	80.8	37.3	100	0-100
SF-36 Energy/Fatigue	73.9	20.9	80	15-100
SF-36 Emotional well being	76.5	19.9	84	28-96
SF-36 Social functioning	80.8	21.7	87.5	25-100
SF-36 Pain	88.9	18.3	100	32.5-100
SF-36 General health	65.6	21.8	70	30-100

Table (8) shows the Sf-36 different parameters for the I pouch patients

3.6.4 The Gastrointestinal Quality of Life Index (GIQLI)

These 5 items concerning bowel habits were answered from the patients and the score of change in bowel habits was calculated. The mean change was 1.6 ± 2.6 and median change was 0 range (-1-10)

3.6.5 Special questionnaire (Tübingen questionnaire)

- Use of vitamin B12

One patient use vitamin B12 supplements (3%) and 32 patients did not require (97%).

- Use of Sodium bicarbonate

13 patients use NAHCO3 (39.4%), while 20 patients do not (60.6%).

- Straining by micturition

22 patients need to strain during micturition (66.7%), while 11 do not (33.3%).

- Urinary tract infection

Only 14 patients experienced postoperative UTI (42.4%). Median number of UTI per year is 0 (0-5). From those 14 patients only 4 experienced ever fever with UTI (12.1%).

- Volume of urine

The patients were asked to roughly estimate the amount of voided urine by each micturition.

The mean volume was 301.5 ± 91.4, (median 250, range 150-550).

- Number of pads used

Mean number of pads used during day time is 1.1 ± 1.3. (Median 1, range 0-5).

Mean number of pads used at night time is 1.1 ± 0.8. (Median 1, range 0-4) (Fig. 28).

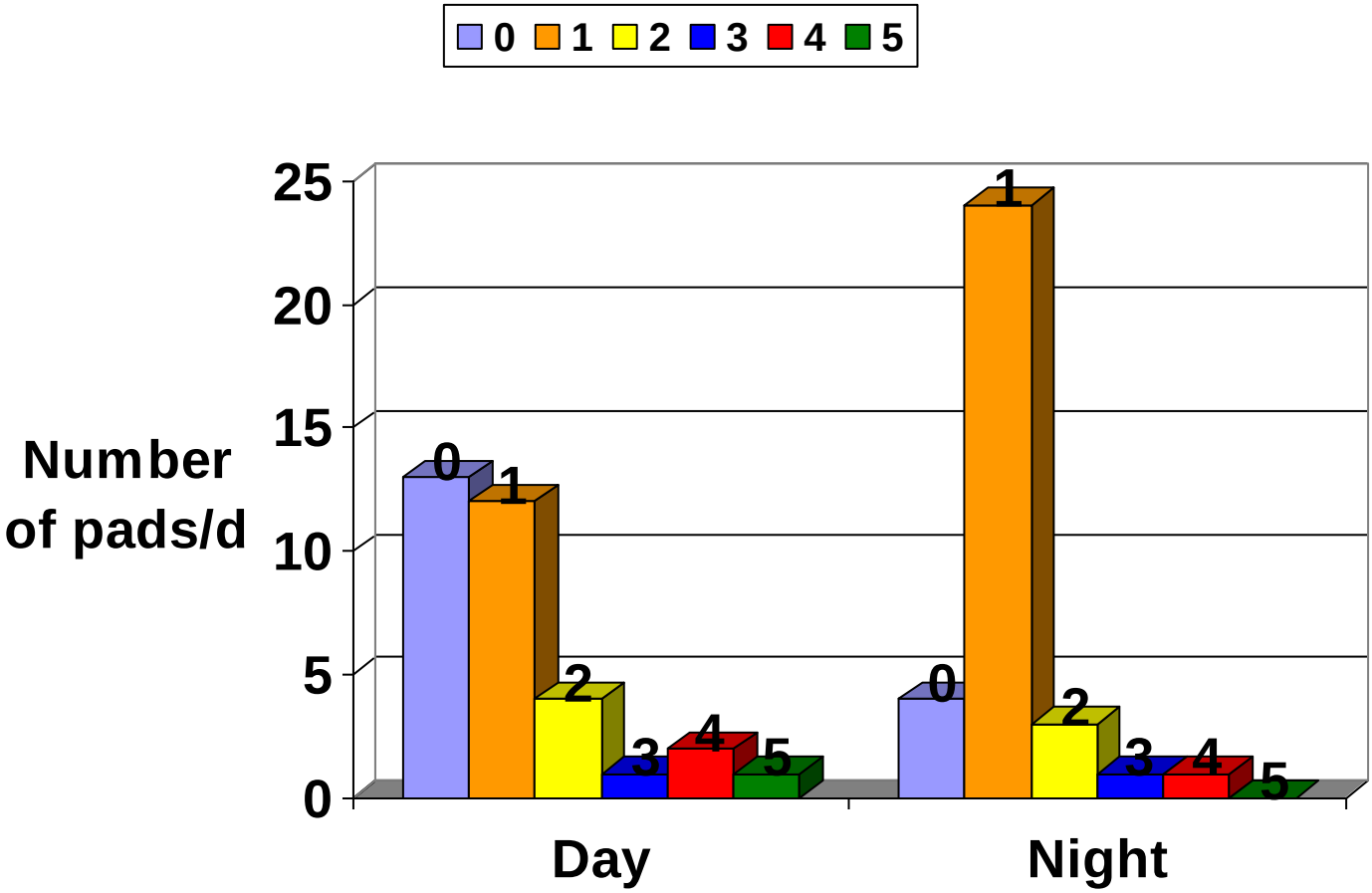

Fig (28) shows number of pad used by the patents day and night

3.7 Urodynamic results:

To verify the results of our questionnaire analysis, patients were asked to undergo urodynamics work-up.

Ten patients accepted to do a complete follow up urodynamics in our department.

3.7.1 Cystometric capacity

The mean cystometric capacity was 445 ± 88 ml, (median 460 ml; range 300-590) (Fig.29).

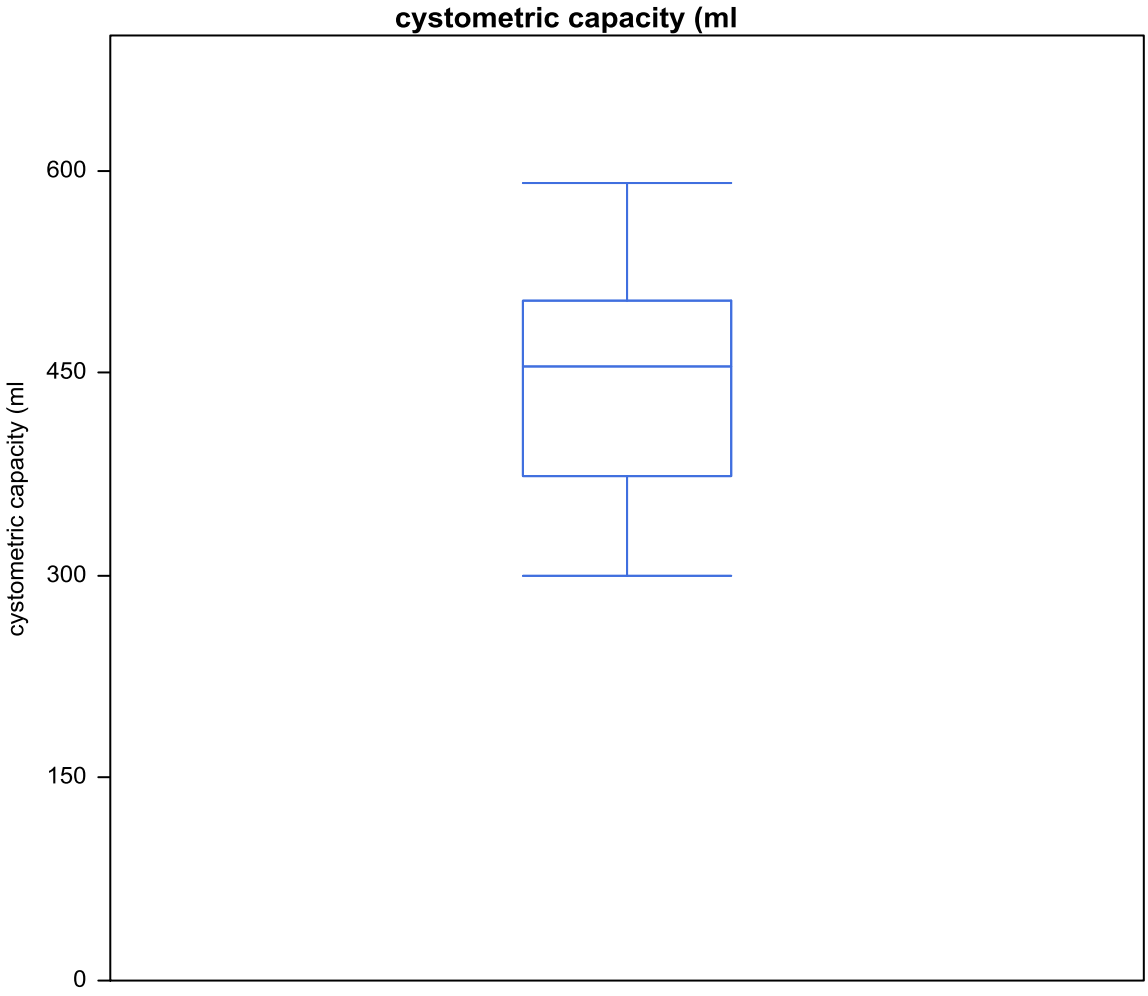

Fig. (29) shows box plot of cystometric capacity. Box represents the range between 25 and 75% percentile of the values and horizontal line represents the mean

3.7.2 Neobladder filling pressure

The mean neobladder pressure at maximum filling was 19 ± 7.9 cmH2O, (median 18 cm H2O; range 5-29) (Fig.30).

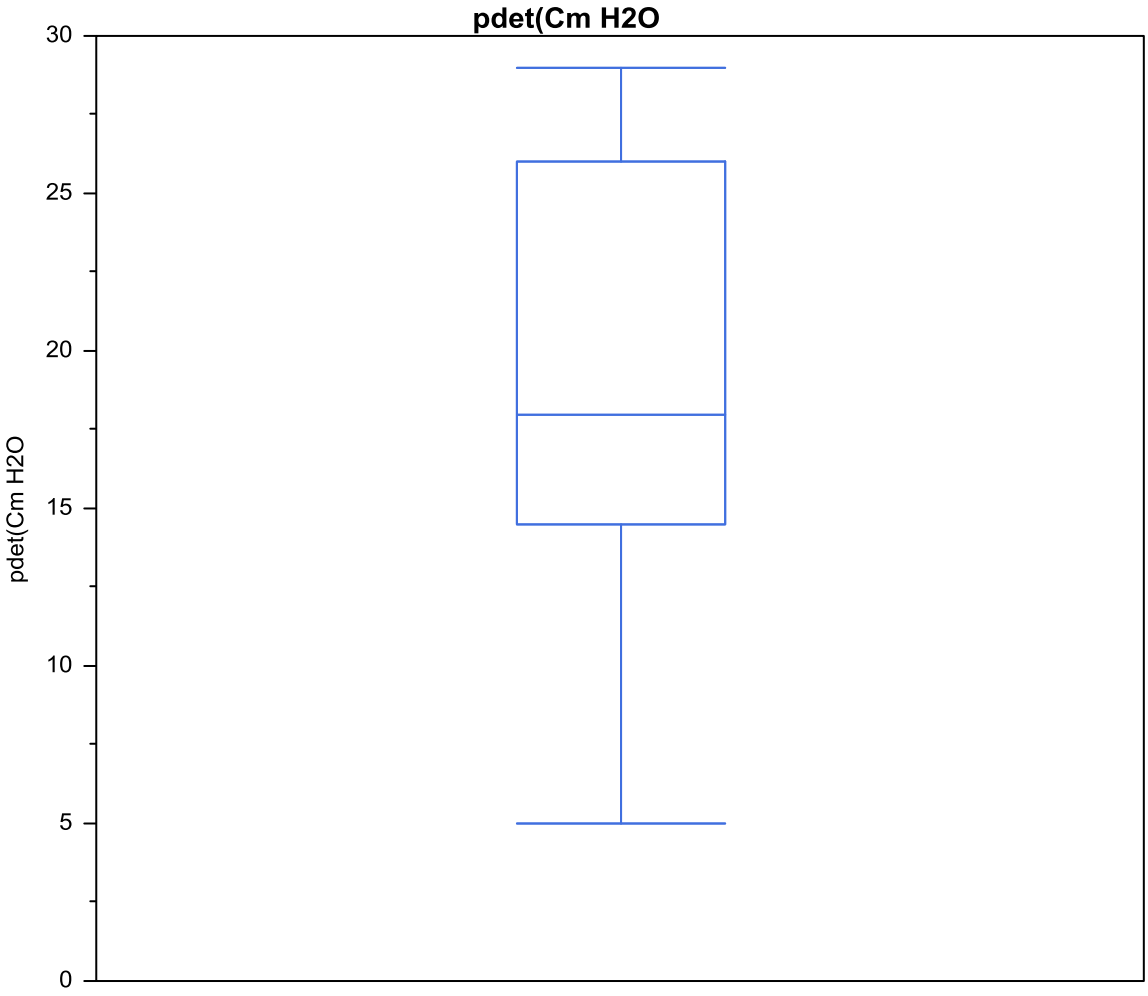

Fig. (30) shows box plot of neobladder pressure at maximum filling. Box represents the range between 25 and 75% percentile of the values and horizontal line represents the mean

3.7.3 Urethral closing pressure

The mean urethral closing pressure was 60.3 ± 36.5 cmH2O and median 55 cmH20 (range 13-142) (Fig. 31).

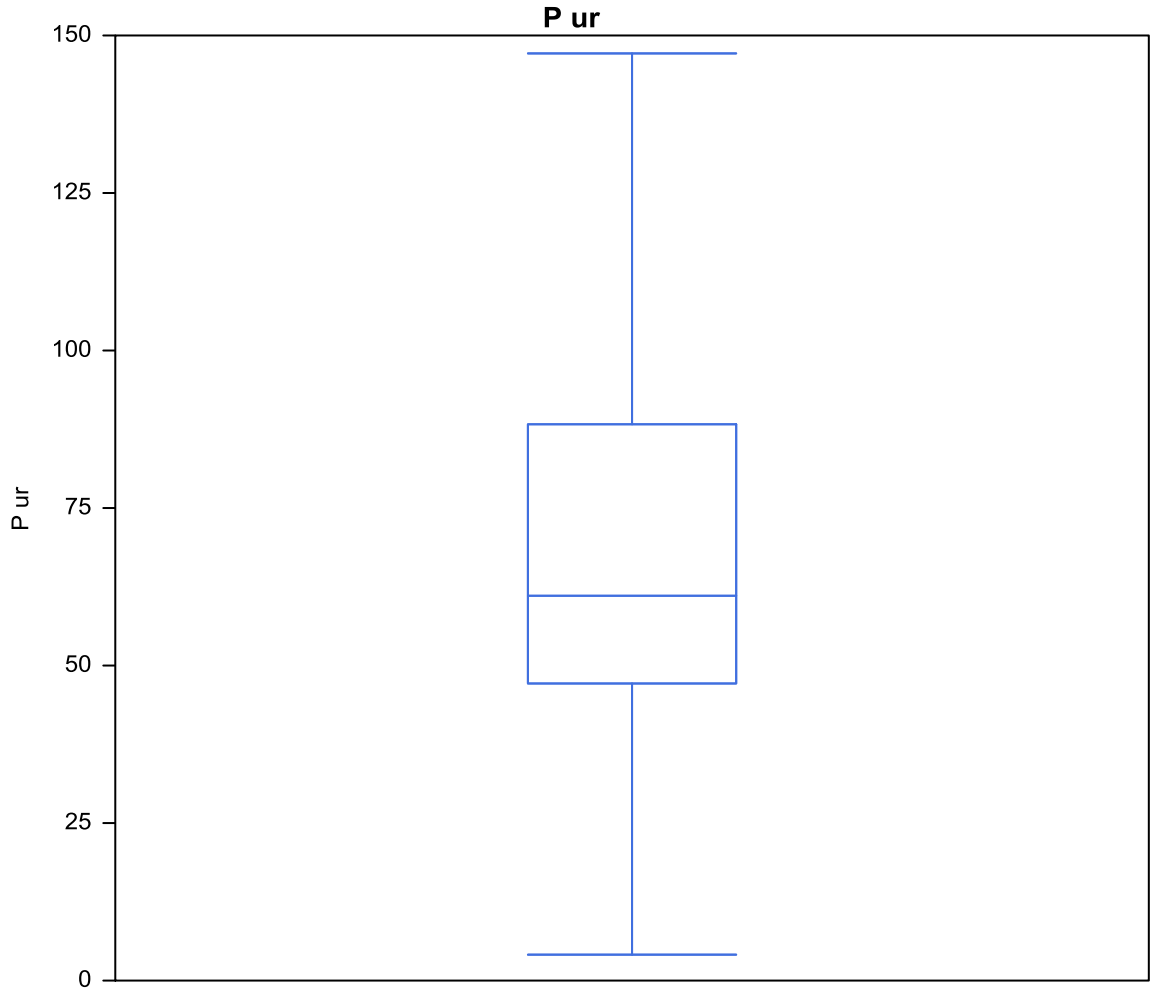

Fig. (31) shows box plot of urethral closing pressure. Box represents the range between 25 and 75% percentile of the values and horizontal line represents the mean

3.7.4 Postmicturition residual urine

The mean volume of postmicturition residual urine was 27.9 ± 53.3 ml and median 15 ml (range 0-170) (Fig. 32).

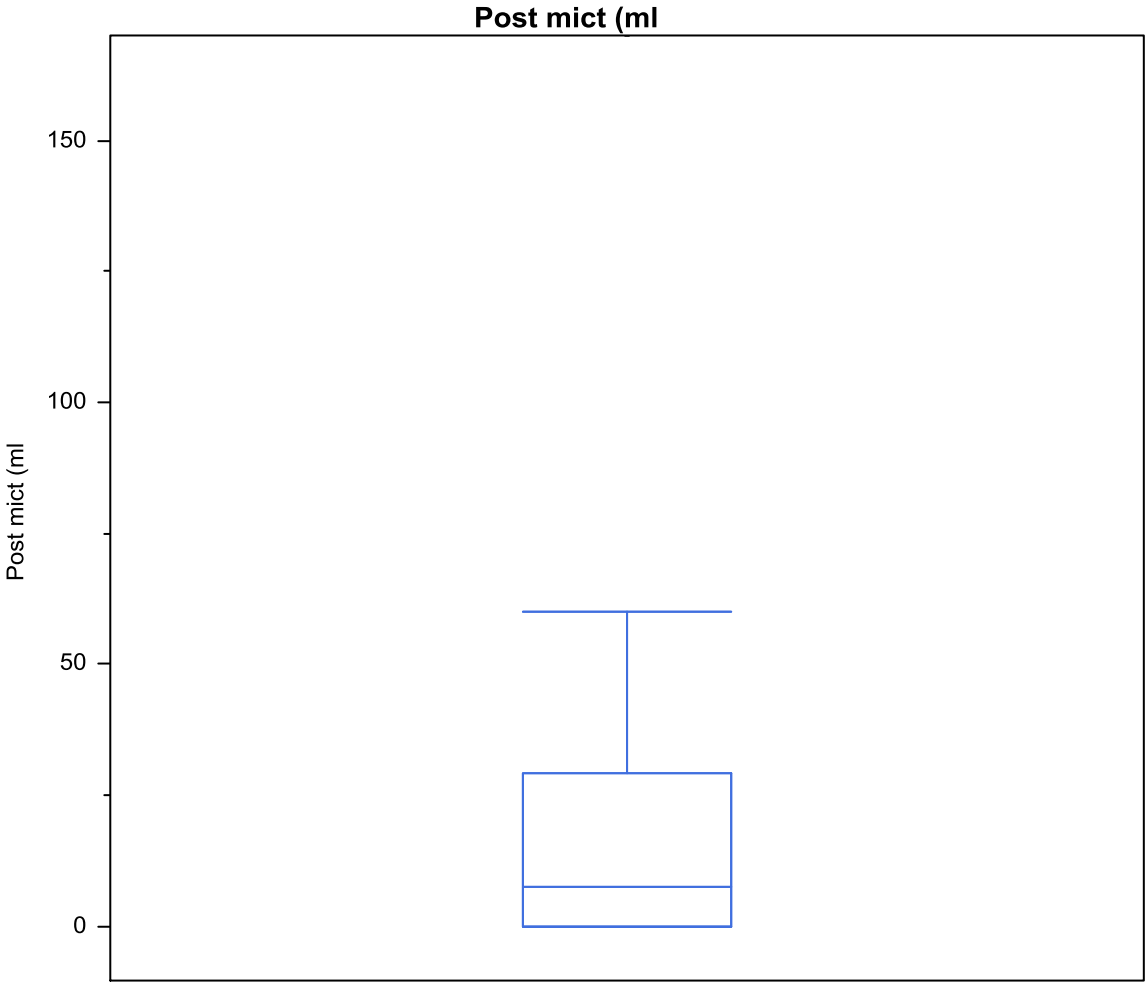

Fig. (32) shows box plot of postmicturition residual urine. Box represents the range between 25 and 75% percentile of the values and horizontal line represents the mean

3.7.5 Vesical pressure during micturition

The mean vesical pressure during micturition was 73.9 ± 25.8 cmH2O and median 73 cm H2O (range 35 -117) (Fig. 33)

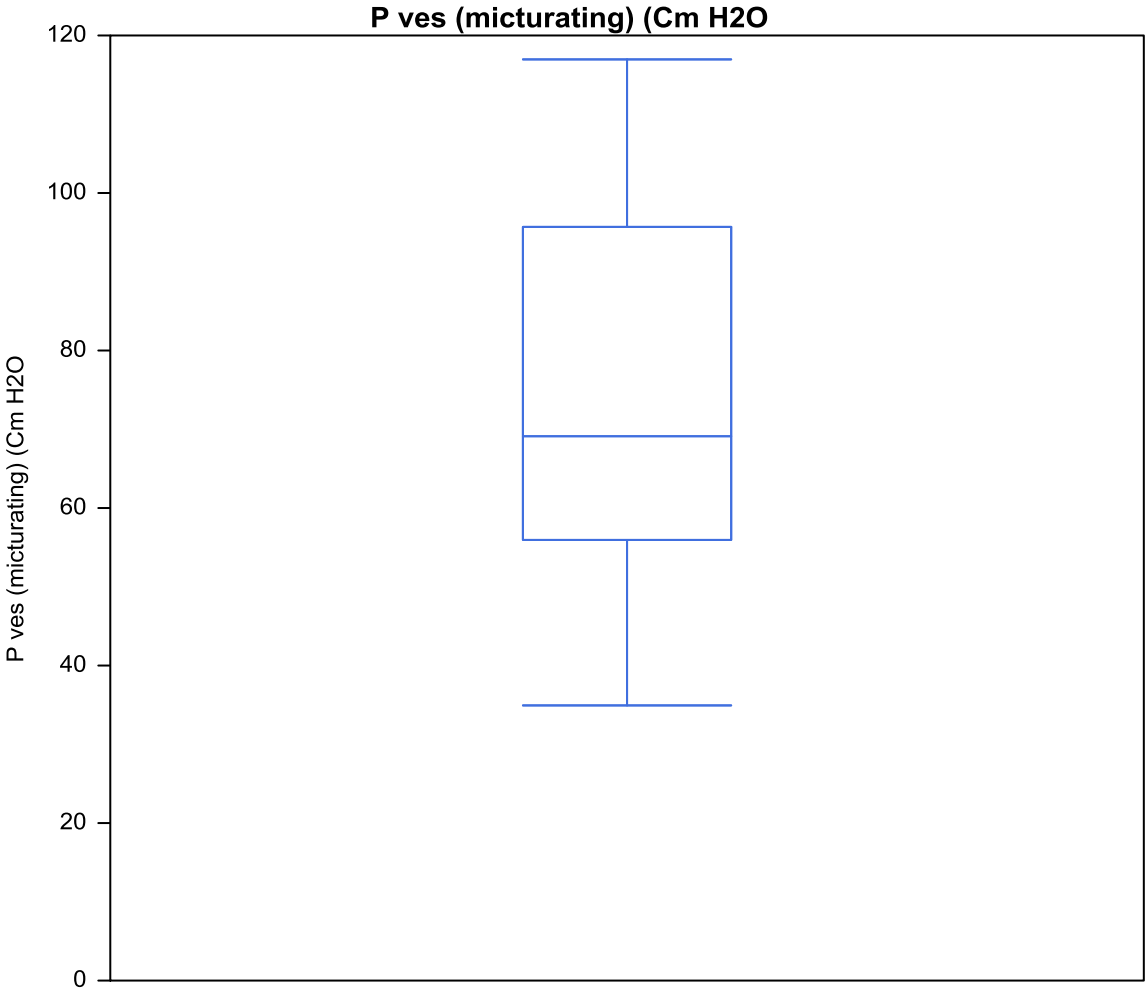

Fig. (33) shows box plot of vesical pressure during micturition. Box represents the range between 25 and 75% percentile of the values and horizontal line represents the mean

4. Discussion:

In this chapter we will discuss the results of the I pouch neobladder as technique of urinary diversion with the results of other ileal neobladders in literature in an attempt to evaluate the outcomes of this new technique regarding oncological and functional aspects.

4.1 Survival

The choice of urinary diversion should not have a major impact on survival, as nerve sparing is only attempted if reasonable from an oncological stand point[74].

Outcome is best characterized by disease-specific survival versus overall survival, which underestimates the impact of treatment in patients with favourable tumour and nodal stage. According to a multi-institutional database of 888 consecutive patients undergoing cystectomy and lymphadenectomy for bladder cancer, mean recurrence-free survival at 5 years was 58% and 66% for bladder cancer-specific survival[42].

The recurrence-free and overall survival in a large single centre study of 1,054 male and female patients was 68% and 66% at 5 years, respectively[29].

In our series the 5 years recurrence free survival, cancer specific and over all survival was 55.1%, 67.9% and 62.2% respectively which are comparable to other series results. In the previous large single centre study it was shown that the 5-yr RFS for patients with organ-confined, lymph node–negative tumours was 85%, and OS was 78%.

The 5-yr RFS and OS for patients with non–organ-confined, lymph node–negative tumours was 58% and 47% respectively[29]. We found that the 5-yr RFS for our patients having organ-confined, lymph node–negative tumours was 70.8 % and the 5-yr OS was 76.4 %. The results of our study are in the same range of other studies either single or multi centre studies regarding the survival. Recent studies showed that recurrence-free survival rates at 2 and 3 years correlate with and are potential intermediate surrogates for 5-year overall survival in patients treated with radical cystectomy for muscle invasive bladder cancer regardless of adjuvant chemotherapy.

The overall agreement between 2-year disease-free survival and 5-year overall survival was 79%, and between 3-year disease-free survival and 5-year

overall survival 81 %[94]. These data were recently externally validated with about 2,500 patients confirming that disease-free survival rates at 2 and 3 years are valid surrogate markers for survival outcome after radical cystectomy[95]. In this study the 2 and 3 years recurrence free survival were 71.4% and 63.2%, respectively, while the 5 years overall survival was 62.2%.

4.2 Complications

Two big issues appear when we discuss the complications of cystectomy and urinary diversion. One is that there is a real lack of standardised reporting of complications after RC; thus, it is almost impossible to compare different series of RC cases. The other is that it may sometimes be difficult to separate the complications arises from each procedure alone[27].

4.2.1 Mortality

There is considerable variability in the mortality rates reported in the urologic literature, with figures ranging from 0.8%[21] to 8.3%[96].Various technical improvements in the surgical and anesthesia techniques, multi disciplinary approach for correction and control of comorbidities and early postoperative rehabilitation have produced salutary effect in reducing the mortality[24]. In our series of 97 patients only 2 (2.1%) patients died in the early postoperative period. The cause of the relatively low mortality rate can be explained by that operations were done in a high center volume by well experienced surgeons. Both factors are known to have great impact on mortality[97].

4.2.2 Morbidity

In an analysis of population-based data, Konety et al. reported at least one complication other than death occurring in 28.4% of patients[98]. However, the observed rate in studies using standardized reporting system is more than double that, reaching between 58% and 64%[22,99]. The total complication rate in our series was 36.1% in the early postoperative period (< 30 days) while it increased to 39.2% in the late postoperative period (< 90 days). Comparison between series of cystectomy with different types of diversion must be viewed cautiously as the patient characteristics differ. However, some series suggest that there are no major differences with regard to early complications between these groups[63].

In a recent study comparing 4 different types of diversions after cystectomy ((1) ileal conduit,(2) Indiana pouch (IP; (3) orthotopic diversions after cystectomy/neobladder, (4) orthotopic neobladders with sexuality-preserving cystectomy), the authors found that 44% of the patients developed early complications (within first 30 days). The complication rate was 48% in Ileal coduit, 43% in Indiana pouch, 42% in neobladder, and 38% in orthotopic neobladders with sexuality-preserving cystectomy. Late complication rate was 51%. The complication rates in the ileal conduit group, Indiana pouch group, orthotopic diversions after cystectomy/neobladder group and orthotopic neobladders with sexuality-preserving cystectomy were 39%, 63%, 59%, and 60% respectively[51].

In order to find a standard way of grading surgical complications the Clavien system seems to be a good solution. The Clavien system for classifying surgical complications was originally described for patients undergoing hepatobiliary surgery and has subsequently been validated in a general surgery population. It is a straightforward and validated instrument that has already been successfully adopted by several urological centers[22,99]. The Clavien system focuses on the therapeutic consequences of a complication, emphasizing the level of intervention required to deal with it[26].

Donat et al applied a modified version of the Clavien system utilized at Memorial Sloan-Kettering Cancer Center to their series of 1142 patients undergoing RC and urinary diversion. 64% of patients had ≥1 complications. Of these 83% were Clavien grade II–V[100].

The main limitation of the Clavien system is that it is less suitable for the reporting of long-term complications[28]. Moreover there might be some subjectivity in how an individual surgeon records complications. Contradictory, the obvious strengths of this system are that it is standardized and has been validated[23].

Most authors now recommend that all complications from urology procedures should be classified according to the modified Clavien system[23].

In our series complications grades were as follow grade I (10.3%), grade II (11.3%) grade IIIA (3.1%) grade IIIB (9.3%), IVA (2.1%), IVB (1%) and V (2.1%).
By considering grade I and II as minor complications 22.6% of our patients had minor complications while 17.6% had major complications. In the largest series of neobladders up to date using the Clavien grading with more than 1000 cases 36% of the patients had minor (grade 1 to 2) and 22% had major (grade 3 to 5)

complications[99]. Therefore these results of the I pouch are comparable to other series.

4.2.3 Blood loss and transfusions

The mean loss ranges from 600–1700 cm3 and blood transfusion rates are about 1–9%[101]. Acute blood loss is common at RC, and predicting blood loss and transfusion requirements remains difficult[102]. In RC, most blood loss occurs when dealing with the bladder vasculature and pedicles[101]. Meticulous intraoperative haemostasis and refinement in surgical techniques is important in order to decrease blood loss[103]. It has been proposed that new technical equipments such as the bipolar device and the harmonic scalpel can be useful[104]. Technical improvement of other fields (i.e., a better technique for dorsal venous plexus ligation) during radical prostatectomy may be associated with decreased transfusion rates seen over time in some cystectomy series[21]. Moreover patient selection and combined epidural and general anaesthesia may continue to lower transfusion rates reported in recent series[105].

In a recent review, LRC or robot-assisted LRC has been shown to reduce the operative blood loss significantly and also the operative time[106].

In our series the transfusion rate was 4.1 %. The following measure are used, controlled hypotensive anaesthesia, various haemostatic surgery devices such as bipolar devices, harmonic scalpel, stapler, oxidised cellulose, absorbable gelatine sponge on raw surfaces, adhesive/biologic tissue glue to minimize blood loss as was recommended by Lawrentschuk and colleagues[101].

4.2.4 Deep vein thrombosis and pulmonary embolism

The rate of deep vein thrombosis ranges from (0.6–5.3%) and pulmonary embolism ranges from (0.7–6%)[101].

Risk factors for deep vein thrombosis (DVT) include age >40 yr, obesity, malignancy, recent surgery, prior history of pulmonary embolism (PE) or DVT, and pelvic lymphocoeles and haematomas[107].

In our series, DVT did not occur while pulmonary embolism rate occurred in one patient 1%. We routinely use low-molecular-weight heparin (LMWH) , advice our patients for early mobilisation and use of compression stockings as recommended[101].

4.2.5 Paralytic ileus

The rate of paralytic ileus ranges from (2.5–22.7%). There is no accepted or standard definition for paralytic ileus but is commonly used to describe temporarily cessation of intestinal motility[101]. Paralytic ileus is commonly observed within 3–5 d after major abdominal surgery. Factors affecting ileus occurrence are type of preoperative bowel preparation, fasting before surgery, intraoperative pain control, hypovolaemia, postoperative pain control, long-term NGT, administration of large amounts of saline and postoperative fasting until recovery of bowel function[108]. Recommendations for prevention are followed like minimization of surgical trauma to the bowel as possible, reduction of analgesic requirements, where possible, beginning of oral fluids on day 1and oral feeding as soon as possible [101].The routine use of nasogastric tube (NGT) is not required following RC, as the time of NGT removal does not affect ileus resolution[109].

Paralytic ileus was defined as transient functional impairment of intestinal motility occurring after surgery. It occurred in 3.1% of our patients.

4.2.6 Wound dehiscence

The rate of Wound dehiscence ranges from (0.5–9%)[101]. A recent meta-analysis suggests interrupted closures with non absorbable sutures to significantly reduce wound dehiscence[110]. In our series wound dehiscence occurred in one patient (1%). Surgeon factors are important, since attention to opposing fascia and correct tension on the suture are of outmost importance, although it is unclear if preemptive tension sutures assist[111]. Significant factors contributing to dehiscence include suture-to-wound length ratio ≥ 4[112], age > 65 yr, wound infection, pulmonary disease, haemodynamic instability, and ostomies in the incision[113]. Treatment recommended for dehiscence involves treatment of sepsis and early repair. Unless the defect is too large, interrupted sutures are preferred over mesh, which should be avoided if any infection is present[114].

4.2.7 Lymphocoele

The rate of lymphocoele ranges from (0.5–3.5%)[101]. In recent years, the extent of lymphadenectomy has increased but without associated rise in morbidity as claimed by specialized centres[115], but there are no prospective studies of the incidence of lymphocele after RC with limited versus extended lymphadenectomy[116].

For decreasing the incidence of lymphoceles, a meticulous surgical technique that includes proper identification and ligation or clipping of lymphatic vessels is required, adequate peritoneal opening for drainage of lymphatic[101]. Decreased lymphorrhoea has also been observed after subcutaneous heparin was administered in the upper arm instead of in the lower half of the body after lymphadenectomy[117].

Lymphocele occurred in 5 patients of our series. Two of them resolved spontaneously while 3 (3.1%) required intervention in the form of percutaneous drainage.

4.2.8 Retention

There is no clear definition for retention but in neobladders, many authors suggest to define retention if residual urine is between 100 ml and 200 ml depending on the type and size of the reservoir[101]. Urinary retention is much more common in women than in men after orthotopic reconstruction. Retention might occur early, but often presents after years of satisfactory neobladder function and emptying[118].

Urethral stricture must be ruled out as a cause of incomplete voiding. The reason for the higher rate of voiding dysfunction in women remains largely unclear. Most investigators assume formation of a ‘‘pouchocele’’ to be the main factor in retention. In their concept, lack of posterior support of the neobladder leads to angulation and obstruction of the neobladder-urethral junction[119]. Studer has proposed that location of the urethral opening in the pouch is an important variable[86]. Chronic retention in orthotopic bladder substitutes may be related to the initial capacity and configuration of the orthotopic bladder substitute pouch at the time of surgery.

In general, causes include angulation of the urethra, elongation of the neobladder neck, position of neobladder neck—not at the lowest portion of pouch, lack of funnelling of neobladder neck during abdominal straining, preserved but dysfunctional native bladder neck, denervated proximal urethra, inadequate pelvic floor relaxation during voiding, neobladder hypercapacity (floppy bag) or ineffective Valsalva straining[23].

It is important to educate and the patient to void the bladder regularly, avoid excessive mucous formation and angulation just proximal to the urethral anastomosis. Successful conservative management may require attempts to reduce

mucous accumulation (e.g., N-acetyl-L-cysteine), prevention of infection, and/or intermittent self-catheterisation[101].

Recent experiences suggest that reducing reservoir capacity by using approximately 40 cm length of bowel rather than 60 cm may contribute to improved voiding function[119]. This was the fact in our series. All our patients did not experience retention in the 90 days postoperative period and only 2 (2.1%) required CIC after the long term follow up. The rate of CIC in other pouches was 7% for Studer[86], 2 % for Mansoura[84] and 5.6% for the Hautmann poch [90]. In a recent long term follow up study for the Hautmann pouch female patients, the rate of CIC was 58 %[120]. This very high percentage of CIC shows the big advantage of the I pouch in which CIC was not required by any female patient.

4.2.9 Rupture (perforation)

Generally, pouch perforation is rare in continent diversion, especially in orthotopic substitutes because outlet resistance is usually low. Rupture can occur spontaneous or during catheterization. The risk may be increased in patients who have had previous abdominal radiation therapy[50].

Rupture can occur due to acute (catheter trauma, mucus retention) or chronic over distention of the neobladder[121]. To decrease risk of rupture due to chronic overdistention, one should emphasize to the patient not to retain urine for long periods and void regularly every 3–4 h, and to remove residual urine at regular intervals[36]. It is a potentially life-threatening complication when it occurs; there are at least two deaths reported in the literature due to pouch perforation of an orthotopic diversion that was unrecognized[50]. This complication did not occur in our series.

4.2.10 Chronic bacteriuria

A positive urine culture is a common finding in patients with urinary diversion (UD), but this does not indicate a symptomatic infection[122] . The incorporation of intestinal segments in the urinary tract helps bacterial growth of the skin flora, anaerobic bacteria, and uropathogenic strains. The bacterial strains growing in the reservoir change spontaneously, indicating colonization rather than infection[119]. As the intestinal neobladders lack the native immunologic defences of the normal bladder mucosa and prostatic secretions, bacterial colonization may progress to invasive tissue level infection more easily in urinary diversion[34].

Risk factors associated with increase bacterial burden are clean intermittent catheterization and residual urine[119]. Recommendations for prevention are to exclude obstruction, avoid residual urine in neobladder and to ensure adequate and constant diuresis[101]. Prophylactic antibiotics are not routinely recommended to reduce risk of drug-resistant bacteria and drug-related adverse effects[36].

The median number of UTI per year in our series was 0, (range 0-2). In the long term follow up only 4 patients out of 33 (12.1 %) experienced symptomatic UTI.

4.2.11 Metabolic complications

The rate of stones in neobladders ranges in the literature from (3.9–9%)[101]. They can occur for many reasons: malabsorption may result in oxalate nephropathy; reabsorption of urine solutes from the reservoir, include acidosis resulting in chronic infections with urease-producing bacteria due to urine alkalosis[123]. In intestinal reservoirs, alterations in bowel mucosa, foreign bodies such as staples or non absorbable suture may also serve as a nidus for stone formation. Finally, alterations in intestinal mucus, particularly in the presence of infection or obstruction, may serve as a nidus or more importantly may interfere with emptying and thereby exacerbate infection and stone formation[124].

Prevention can be aided by preserving the most distal 10– 25 cm of ileum and—postoperatively[125], by ensuring adequate reservoir size, ensure hydration and emptying of the reservoir reduce the risk of bacteriuria (In this respect angulation of conduit should be avoided and encouraged frequent voiding to ensure minimal residual volumes)[101]. Patients should be encouraged to ensure hydration and frequently void their neobladder to minimize residual volumes, risk of UTI and bacteruria. However, treatment of UTI and bacteriuria if the urine is sterile is controversial since about 40% of patients with an orthotopic bladder will have persistent bacteriuria and may have other adverse affects, such as resistant organisms[125].

No single case in our series experienced stones at any time of follow up. Various electrolyte disturbances can occur based on which segment of the gastro-intestinal tract is chosen for urinary reconstruction: stomach, jejunum, ileum, or colon[126]. The electrolyte abnormality that occurs with the ileum and colon is hyperchloremic metabolic acidosis[51].

The mechanism of hyperchloremic metabolic acidosis is due to the ionized transport of ammonium. Ammonium substitutes for sodium in the Na+-H+ antiport. The exchange of the weak acid NH4 for a proton is coupled with the exchange of bicarbonate for chloride. Thus ammonium chloride is absorbed across the lumen into the blood in exchange for carbonic acid (i.e., CO2 and water). Ammonium also gain entry to the blood from bowel lumen through potassium channels[127].

Hyperchloremic acidosis is most prevalent following ureterosigmoidostomy. Chloride absorption and bicarbonate excretion are more pronounced in the colon. Therefore, it is preferable to use ileum rather than colon for bladder reconstruction to reduce the risk of hyperchloremic acidosis, specially in the presence of renal impairment[23]. Whichever segment of bowel is used, regular voiding and drainage to completion are important to diminish electrolyte imbalances[75]. This also did not occur in our series. The potassium depletion is due to renal potassium wasting as a consequence of renal damage, osmotic diuresis, and gut loss through intestinal secretion. Patients with ureterocolonic diversions are more expected to have hypokaleamia than those with ileal diversions[128]. We observed only a rate of 3.1 % in our patients.

Malabsorptive vitamin B12 deficiency may be a concern and a relatively uncommon problem[129]. Distal terminal ileum preservation is essential, and it may take 3–4 yr to deplete hepatic vitamin B12 stores. Chronic vitamin B12 deficiency is insidious and may result in irreversible neurologic and hematologic sequelae[34].

In the long term follow up questionnaire of our 33 patients only one patient (3 %) reported to require vitamin B 12 supplements.

4.3 Upper tract obstruction:

Obstruction may be benign or malignant (a second primary site or a recurrence at the ureterointestinal anastomosis). Malignant recurrences at the ureteroileal anastamoses are considered to be late oncological events after radical cystectomy occurring after a median follow up time of 36 months[9]. Benign strictures commonly occur during postoperative year 1 and are usually asymptomatic because they develop slowly[101]. The type of ureteroileal anastomosis (Bricker vs Wallace) does not affect the stricture incidence[80].

The primary cause of uretero-intestinal stenosis is ischemia. When dissecting the ureters at the time of radical cystectomy, it is important to avoid devascularization of the distal ureteric segment which is to be reimplanted[119].

Meticulous handling and preparation of the distal ureter are essential to minimising the risk of urine leak and postoperative stricture. Moreover ensuring good vascular supply, limiting the dissection, adequate calibre ureteroenteric water tight anastomosis, complete excision of pathologic lesions, good drainage, and a wide spatulated and tension-free anastomosis of mucosa to mucosa remain of paramount importance [69]. It is also important not to angulate the ureter during reconstruction as that can also lead to postoperative obstruction[119].

Early diagnosis and prompt drainage (usually with a nephrostomy) are required to prevent consequent renal parenchymal loss and infectious complications[130]. Although endoscopic and percutaneous management procedures are established treatment options, open surgical revision may need to be the long-term definitive treatment, particularly if the stricture occurs after 6 months[51]. The rate of Upper tract obstruction differs in different types of orthotopic diversions mainly due to the type of ureteric implantation in the newly formed neobladder. It can be understandable that a refluxing implantation has a less chance to be obstructed than implantations which include an antireflux technique. In a randomised trial tunnelling techniques for antireflux mechanisms carried a higher risk of stenosis[131]. The rate of ureteroileal stenosis for different types of neobladder was 2.7 % for Studer neobladder, 9.3% for Hautmann neobladder, 3.8 % for the serous lined extramural tunnel (El mansoura pouch) and 10 % for the T pouch ileal neobladder[84,86,90,132]. One of the major problems in comparing the results of different techniques of neobladders regarding obstruction is that there is no standard definition for it. In our series we differentiated between 3 types of clinical obstruction and hence different percentage according to each type. Sixteen and half (16.5 %) of all our patients had obstruction at any time during the follow up.

This percentage decreased to 7.2 % after exclusion of the patients that required no treatment (they experienced hydronephrosis at a certain point that was self limited and spontaneously resolved). The percentage was 2.1 % after excluding the patients that required only PCN tube or JJ stent as a temporary treatment for hydronephrosis and include only the patients that required a definitive surgical treatment in term of open reimplantation or endourological uretrotomies. Thus with a

2.1 % of true obstruction our antireflux technique of ureteral implantation in a subserosal tunnel after anastamosing both ureters together with the modified Wallce technique seems to be comparable with other techniques of neobladders. Anastamoses of the ureter to the posterior wall of the neobladder also gives an advantage of placing the ureters in an easily accessible place for a possible later on endoscopy of the upper tract. The main advantage of the antireflux technique is to protect the upper tract from deterioration by preventing reflux. In our series only 1 (1%) patient had postoperative reflux detected by postoperative retrograde cystography. These results are better than other techniques both using refluxing or antireflux anastamoses, The reflux rate for Hautmann was (3.3%), Mansoura (3%) and the T pouch 10 %[84,90,132].

Although techniques using antirefluxing mechanisms are still used for ureterosigmoidostomy or continent reservoirs with a catheterisable abdominal stoma due to higher intraluminal pressures, the evidence for its use in orthotopic bladder substitutes is equivocal[34]. Other causes of renal deterioration are chronic retention, infection due to inadequate catheterization, poor compliance, and high storage pressure in the reservoir and subsequent reflux[119]. Another cause of avoiding renal deterioration is the use of only 40 cm for the formation of an ileal reservoir as this decreases the surface area of the neobladder that is exposed to urinary constitutes and thus decreases their absorption through the bowel mucosa.

4.4 Incontinence:

Multiple factors influence continence including patient age and mental status, an intact and innervated urethral sphincter, urethral length, surgical technique, low-pressure/large-capacity reservoir (>300 ml), absence of bacteriuria, and completeness of voiding[23,36]. Continence usually improves within the first 6 to 12 months postoperatively as the compliance of the reservoir increases allowing storage of greater volume at lower pressure. Patients learn to void by performing a Valsalva maneuver in coordination with relaxation of the pelvic floor, resulting in spontaneous voiding to empty the pouch. Daytime continence is often achieved before night-time continence[119]. The various studies have demonstrated rates of good or excellent daytime continence at 85–90%, defined as totally dry or use of one pad per day after 12 month from surgery[34]. El Bahnasawy et al found rates of enuresis ranging from

27% to 50% for follow-up intervals more than 12 months in male patients with hemi-Kock or Hautmann ileal neobladder[133].

Persistent severe incontinence is a difficult clinical problem. To decrease the risk of incontinence a more meticulous dissection around the prostatic apex with less damage to the external sphincter mechanism and membranous urethra is required[36]. Nerve-sparing cystectomy is significantly associated with improved continence rates[134]. Possible treatment strategies for incontinence are intermittent self-catheterization, augmentation of the neobladder, peri-urethral collagen injection, placement of a urethral sling or implantation of an artificial urinary sphincter. Some patients may even need removal of the neobladder and cutaneous diversion. Pharmacotherapy is of little or no value[119].

The main obstacle of objective evaluation of continence with continent reservoirs is that it varies across series due to different methodology including subjective and objective definition of degrees of continence determined at different time points from surgery. It is recommended to assess continence by stratifying into daytime versus nocturnal incontinence[36]. The rate of day incontinence varies in different series of cystectomies according to the technique and the way of definition of incontinence. In a long term follow up study up to 20 years Studer and associates found that daytime continence improved quickly and reached a plateau 12 months after surgery. They noticed that this percentage remained stable for 7 years[86].

For the Studer neobladder they reported day continence rate reaching 92 % and nocturnal incontinence up to 79 %. Continence was defined according to the amount of urine loss as follow: continent = No single drop loss, loss of 5 to 10 ml daily, loss of less than 1 dl daily, loss of less than 2 dl daily and loss of more than 2 dl daily[86].

Another way of defining continence used for evaluation of the Hautmann neobladder with 11 years follow is as follow .They divide continence into 3 grades (good, satisfactory and incontinent). They included in the good group those patients that were either completely dry without use of pads for protection or the completely dry with the use of one pad reaching a rate of day time continence up to 83.7 % and night continence up to 66.3 %. They consider patients that use no more than one pad daily which gets wet as satisfactory continence which raised their results to reach (95.9 % and 95 %) for day and night continence respectively[90].

For the Mansoura group, they did not define the day continence but define the night continence as patients that not use pads or medication and had a night time frequency of 2 voids or less. The continence rate was 93.3% and 80% for day and night, respectively[84]. In our series the continence rate at long term follow up for the group of patients that answer the questionnaire was 75.8 % and 84.9 % for day and night continence respectively. (Continence was defined as patients that are completely dry or using one pad for protection). This percentage increased to 80 and 90 % for day and night continence after including only the patients that underwent a nerve sparing radical cystectomy.

One might think that the relatively lower continence rate in our series might be attributed to the decreased bladder capacity due to the use of only 40 cm of ileum in its reconstruction. However this is not the fact as bladder capacity detected by urodynamic studies showed that it is comparable with the other forms of neobladders even those using 60 cm from the bowel. Another contributing factor is that nerve sparing cystectomy was not oncologically feasible in one third of the patients. By contrast the high night continence rate underlines that the capacity of I pouch is high enough to store large volume of urine at night.

4.5 Quality of life:

The published literature on quality of life (QOL) after radical cystectomy is rather extensive. However, the scientific quality is low. In 2005 by Porter et al[135] performed a systemic review of a total of 378 studies Based on their inclusion criteria (adult patients, bladder cancer, comparative studies, original research, primary study outcome related to QoL, use of defined QoL instruments), only 15 of these 378 studies were appropriate for analysis. Moreover, no randomized controlled study has been undertaken, which would be desirable but probably difficult to conduct. Only one study was prospective. Only two-thirds used validated QoL instruments, and only 73% used bladder cancer disease-specific instruments. Although two studies have shown a statistically significant difference in QoL in favor of neo-bladders[136,137]. Published evidence does not support an advantage of one type of reconstruction over the other with regard to QOL. The reason for such results may be that patients are subjected preoperatively to method-to patient matching and therefore they are prepared for disadvantages and advantages associated with different methods[34]. In our series we used many types of questionnaire in an attempt to evaluate different

parameters of quality of life. We use the SF-36 as a general questionnaire type. In our series the results of different items of SF 36 questionnaire are high ranging from 65.5 for general health status, 88.9 for presence of body pain.

SF-36 Physical functioning (PF) was 78.2 ,SF-36 Role of limitation due to physical health (RP) 76.5, SF-36 Role of limitation due to emotional problems (RE) 80.8, SF-36 Social functioning (SF) 80.8, SF-36 Body Pain (BP) 88.9 and SF-36 General health (GH) 65.6. A Japanese group performed the SF-36 questionnaire analysis for different types of orthotopic reservoirs and also for an age matched control group[138]. The results for different Items of SF-36 for the studer pouch, Hautmann pouch and the control group were considerably lower with rates of 47.6, 47.6, 47.7 for PF, 46.8, 46.4, 48.8 for RP, 51.1, 51.8, 49.7 for BP, 48.9, 49.5, 49.6 for GH, 47.9, 48.7, 49.6 for SF, 44.1, 44.3, 49.8 for RE respectively. In the view of these results, all the SF-36 parameters by I pouch patients was better than parameters of patients with Studer and Hautmann puoches done by this Japanese group.

In another group from United Kingdom[136] used the SF-36 questionnaire to compare the quality of life between patients with ileal conduit and patients with orthotpic diversions the results were as follow for different parameters. Orthotopic neobladder SF-36 results were 77.4 for (PF), 68.5 for (RP), 86.5 for (RE), 79.2 for (SF), 78.3 for (BP) and 73.8 for (GH). Ileal conduit diversion SF-36 results were 61.8 for (PF), 59.8 for (RP), 79.0 for (RE), 79.7 for (SF), 81.4 for (BP) and 68.2 for (GH). From these results it is obvious that the patients in our series receiving I pouch as the type of diversion have apparently a comparable quality of life to other forms of diversions and also to ileal conduit patients.

The QLQ- C30 was used as a cancer specific questionnaire. In our series the score of the global health status was 75.2 ± 20.5 and the quality of life score was 73.2 ± 19.5. The quality of life of our patients seems to be slightly higher than in other mentioned groups. In a recent German QLQ-30 questionnaire study in more than 100 cases of cystectomy, the global health status/quality of life score for patients underwent cystectomy and neobladder formation according to Hautmann were (72.3 ± 19.5) while for those underwent cystectomy and ileal conduit it was (58.0 ± 25.3 **)** with the difference to be statistically significant[139]. In another Japanese group the global health status/quality of life score for patients underwent cystectomy and ortotopic diversions was also 72[140]. QLQ-BLM 30 was used in our study as bladder

cancer–specific questionnaire specific for muscle invasive bladder cancer patients undergoing cystectomy and urinary diversion because this type of questionnaire was recently validated in some studies. In the German study[139] applying the Hautmann pouch as diversion for their cystectomy patients the mean score of the urinary symptoms was 33.6 ± 26.3 while our mean score was 32.2 ± 20.2 which is slightly lower keeping in mind that a higher score indicates a worse symptomatology.

The five questions concerning bowel habits from the Gastrointestinal Quality of Life Index (GIQLI) were used to evaluate the change that occurred due to the operation. This questionnaire was used for the first time by Fung and his colleges[93]. They found that there was no change in the bowel habits preoperatively and for 2 years follow up in patients undergoing the Studer ileal neobladder as the type of diversion after cystectomy. In our series the median change of bowel habits pre and postoperatively was 0. Therefore we can assume that the technique of the I pouch neobladder by using only 40 cm from the intestine has no negative impact on bowel habits postoperatively.

4.6 Sexual function:

RC may be associated with sexual dysfunction in both men and women. Erectile impairment in males after RC is more extensively described in the literature than female sexual dysfunction[141,142].

For men, even when the operation is performed by skilled and experienced surgeons after meticulous nerve sparing dissection, preservation of normal sexual function is only 50%[134]. Preservation of the whole or part of the prostate and/or seminal vesicles has been proposed to attain a higher potency rate of 75% to 100%[143]. However the problems with such procedures are increased recurrence rate and chronic urinary retention rate, probably related to prostatic remnants. Moreover, the risk of prostate cancer remains unchanged[144].

This type of surgery should be done only in specially selected patients who are relatively young, sexually active with organ-confined bladder tumour without high risk of subsequent urethral recurrence[30]. All aspects of female sexuality may remain unchanged following cystectomy and ileal neobladder formation as long as sexual activity is not ceased due to other reasons[142]. The functional length of the vagina is probably less important, although an intraoperative length of >12 cm measured during surgery has been. Retubularisation of the vagina done in a longitudinal

fashion can cause dyspareunia if it results in lumen narrowing; hence, closing the vagina transversely might be more appropriate[145]. Only half of female patients have successful sexual intercourse after RC; factors that might attribute to this are reduced vaginal lubrication caused by damage to autonomic nerves originating from the hypogastric plexus, inability to have orgasms, decreased sexual desire, and dyspareunia[142]. Another small study has compared nerve sparing and non–nerve-sparing cystectomy in females and found that preservation of female sexual function was more pronounced in patients who received neurovascular preservation surgery[146].

Regarding the sexual function in the group of patents with answered questionnaire 63.6% (69.2% for men and 42.9% for women) of our patients remained sexually active postoperatively while 26.4% lost their sexual function. A larger study with 101 male patients reporting potency rate of 62% in men 49 years and younger[147]. In a larger group of patients with 20 years of follow up an overall potency rate of 37.8% was reported[86]. Recently a Japanese group showed that most of their patients (88%) had lost sexual function after radical cystectomy and orthotopic neobladder[148]. The Ulm group reported that 58.6% of their female patients remained sexually active postoperatively. In view of these results, our results show that a high percent of our patients retain their sexual function postoperatively.

4.7 Urodynamics:

An intact sphincteric mechanism, adequate bladder capacity, absence of uninhibited contractions and good compliance are the main features determining the neobladder function and continence.

The importance of studying the urodynamic characters of orthotopic reservoirs is that the volitional voiding via the urethra and continence are considered the most important factors determining a good quality of life for these patients[149].

In a study comparing three different neobladders using different parts of the intestine (ileal, ileocecal and sigmoid) urodynamicaly, they found no significant differences between them regarding the maximal capacity and the neobladder volume, the pressure at the maximal capacity, the pressure at maximal flow, the post void residual and the maximal flow[150].

For the urodynamically analyzed group of our patients, cystometric capacity was 445.4 ± 86.5 ml. (median 455, range 300-590). In a study evaluating urodynamic

characters of asymptomatic males the mean cystometric capacity was 329 ± 15 ml[151]. By contrast the median cystometric capacity of the 60 cm ileal Hautmann neobladder was 480 ml (370–806)[152]. .A Turkish group evaluated the Hautmann pouch after modifying the length of the bowel to 40 cm only, the neobladder capacity of their patients reach to 330 ml after 6 months and to 550 ml after 18 months of follow up[153]. The Studer pouch using 60 cm from the bowel but only 40 cm for the pouch itself showed a cystometric capacity of 420 ml after a follow up of about 5 years[154]. The PADUA pouch (40 cm from bowel shaped to a reservoir in an inner circle manner) was evaluated urodynamically 1 and 4 years after cystectomy. The 4 years cystometric capacity was reported to be 544 ± 95 ml[149].

Theoretically, making the reservoir from a larger segment of bowel, e.g. 60 cm appears to be a good solution, as with a 50% increase in bowel surface almost double the capacity can be obtained. Initially results do appear better with longer micturition intervals and better postoperative continence. However, the advantage is only temporary and a floppy bag may develop with increased risk of chronically infected residual urine and high risk for lifelong intermittent self-catheterisation[74].

These findings showed that the I pouch using only 40 cm from the intestine has a very good capacity in comparison to normal population or other types of ileal orthotopic diversions and that the use of smaller length from ileum has no obvious effect on the final capacity in the long term period. In the Hautmann pouch the median residual volume was 10 ml, 15 ml for the Studer pouch and 50 ml for the PADUA pouch[149,152,154]. The mean residual volume for the study group of our patients was 28 ± 53 ml. This makes the functional capacity (cystometric capacity- residual urine) of our neobladder of about 420 ml. Moreover the rate of CIC usage was only 2.1 % which is considerably lower than that of other techniques with 7% for Studer and 5.6 % for the Hautmann reservoir[86,90].

Compliance describes the change in volume over a related change in reservoir pressure. During normal filling of the intestinal reservoir little or no pressure changes occurs to have a normal or low compliant pouch. There is no standard for what is normal, low or high compliance[155].

The mean end filling pressure of the I pouch was 19 ± 7.9 cmH2O while the median for the Hautmann pouch was 16, 26 for the modified Hautmann pouch and 18 for the PADUA and Studer pouches[90,153]. In view of these results the urodynamic parameters of the I pouch are comparable to other orthoptopic neobladders.

Limitations of this study include the relatively small sample size, the relatively short follow up time, the continence rates depend on questionnaire analysis with subsequent effect from subjectivity. However many Items were in favour of the I pouch as the use of only 40 cm of the bowel, the low obstruction and reflux rates, the low rate of the CIC use, the satisfactory neobladder capacity and the relatively high quality of life.

5. Conclusion

Based on the results of this interim analysis, the functional, oncological and perioperative outcomes of the “I-pouch” neobladder technique are comparable to other established ileal neobladder techniques. Although using an antireflux technique of ureteral implantation, the ureterointestinal stenosis rate is only 2 %. Even though we use only 40 cm from the terminal ileum to create the pouch, the final neobladder capacity are comparable to those using longer bowel segment.

The quality of life of patients with I pouch is good reaching in some cases the quality of life of the normal population. In addition, the differences to other ileal reservoirs are that the length of ileum is reduced to 40 cm with subsequent less complication on the gastrointestinal tract and that the directly implanted ureters lie on the dorsal wall of the pouch which facilitates instrumentation of the upper tract at a later point. Further prospective randomized controlled studies are needed to compare the results of I pouch to other types of orthotopic diversions to know if there is one type is superior to the others. However this will be hardly to prove.

6. Summary

There are many factors affect the choice of the urinary diversion after cystectomy which are either cancer-related or patient-related. Orthotopic diversion is the preferred urinary shunt whenever possible and ilieum is the most used part of the bowel. There are many types of neobladders that were developed in an attempt to reach a perfect solution for urinary diversion. A newly developed neobladder by Department of Urology in Tübingen (the “I pouch”) was extensively studied in this thesis regarding the perioperative, functional and oncological outcomes.

In this study 97 patients that underwent radical cystectomy and I pouch as a urinary diversion between January 1999 until August 2011 were included. All preoperative and postoperative parameters were recorded as age, sex, serum creatinine, pathology of the tumor, presence of metastasis and complications in which we used a special grading system (Clavien grading) to categorize complications and to be better compared with other techniques in literature. The follow up of these patients reach more than 40 month. The presence and absence of recurrence was also recorded and the survival rates of the patients. All alive patients were contacted to do questionnaires evaluating the quality of life after the operation and more than one third of the patients answered them. The used questionnaires were the (SF-36) as general questionnaire, the (QLQ-C30 version 3) as a cancer-specific questionnaire, the (QLQ-BLM30) as disease specific for invasive bladder cancer, 5 questions from the Gastrointestinal Quality of Life Index to asses the bowel habits changes after the operation and a specific self developed questionnaire of the department to evaluate the items thought to be missed by the other questionnaires. Moreover 10 patients accepted to do follow up urodynamic study which was done to evaluate objectively parameters as cystometric capacity of the newly formed bladder, the pressure inside the pouch during filling and during evacuation, the uroflow, the urethral closing pressure and the presence or absence of postmicturition residual urine.

It appears that neither the I pouch nor any other pouch has clear superiority over the other types. Each type has advantages and disadvantages. The advantages of the I pouch that it uses only 40 cm from the ileum with no effect on the final capacity of the pouch reaching about 450 ml. Although an antireflux technique of ureter reimplantaion was used, this did not increase the upper urinary tract obstruction rate which was only (2.1 %) that was even smaller than other orthotopic

neobadders using a refluxing mechanism oh ureter implantation as Studer and Hautmann pouches. Indeed the rate of reflux was only 1% which helps in avoiding deterioration of the renal function. The bowel habits in patients with I pouch were not affected. The sexual function was preserved in about 64 % of our patients after the operation which is considered high rate in comparison with other series in the literature. The quality of life of patients with I pouch is good reaching in some cases the quality of life range of the normal population. The disadvantage of the I pouch is the some what low continence rates specially at the day time which can not be explained in terms of low capacity.

The perioperative, oncological and functional outcomes of the I pouch are comparable to other well known established techniques like the Studer, Hautmann, Mansoura and T pouches.

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8. List of tables

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10. List of abbreviation

ASA	American Society of Anesthesiologists
BC	Bladder cancer
BP	SF-36 Body Pain
CIC	Clean intermittent catheterization
CIS	Carcinoma in situ
DVT	Deep venous thrombosis
EORTC	European Organisation for Research and Treatment of Cancer
GH	SF-36 General health
HRQoL	Health related quality of life
JJ	double J stent
LMWH	low-molecular-weight heparin
LN	Lymph node
LRC	Laparoscopic radical cystectomy
NGT	Nasogastric tube
OBS	Orthotopic bladder substitution
OS	Overall survival
PCN	Percutaneous nephrostomy tube
PE	Pulmonary embolism
PF	SF-36 Physical functioning
QoL	Quality of life
RC	Radical cystectomy
RE	SF-36 Role of limitation due to emotional problems
RFS	Recurrence free survival
RP	SF-36 Role of limitation due to physical health
SF	SF-36 Social functioning
UD	Urinary diversion
UTI	Urinary tract infection

11. Acknowledgement

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EORTC QLQ-C30 (version 3.0)

Wir sind an einigen Angaben interessiert, die Sie und Ihre Gesundheit betreffen. Bitte beantworten Sie die folgenden Fragen selbst, indem Sie die Zahl ankreuzen, die am besten auf Sie zutrifft. Es gibt keine "richtigen" oder "falschen" Antworten. Ihre Angaben werden streng vertraulich behandelt.

Bitte tragen Sie Ihre Initialen ein: ____

Ihr Geburtstag (Tag, Monat, Jahr): __ __ __ __ __ __

Das heutige Datum (Tag, Monat, Jahr): 31 __ __ __ __ __ __

		Überhaupt nicht	Wenig	Mäßig	Sehr
1.	Bereitet es Ihnen Schwierigkeiten sich körperlich anzustrengen (z.B. eine schwere Einkaufstasche oder einen Koffer zu tragen?)	1	2	3	4
2.	Bereitet es Ihnen Schwierigkeiten, einen längeren Spaziergang zu machen?	1	2	3	4
3.	Bereitet es Ihnen Schwierigkeiten, eine kurze Strecke außer Haus zu gehen?	1	2	3	4
4.	Müssen Sie tagsüber im Bett liegen oder in einem Sessel sitzen?	1	2	3	4
5.	Brauchen Sie Hilfe beim Essen, Anziehen, Waschen oder Benutzen der Toilette?	1	2	3	4

Während der letzten Woche:

		Überhaupt nicht	Wenig	Mäßig	Sehr
6.	Waren Sie bei Ihrer Arbeit oder bei anderen tagtäglichen Beschäftigungen eingeschränkt?	1	2	3	4
7.	Waren Sie bei Ihren Hobbys oder anderen Freizeitbeschäftigungen eingeschränkt?	1	2	3	4
8.	Waren Sie kurzatmig?	1	2	3	4
9.	Hatten Sie Schmerzen?	1	2	3	4
10.	Mussten Sie sich ausruhen?	1	2	3	4
11.	Hatten Sie Schlafstörungen?	1	2	3	4
12.	Fühlten Sie sich schwach?	1	2	3	4
13.	Hatten Sie Appetitmangel?	1	2	3	4
14.	War Ihnen übel?	1	2	3	4
15.	Haben Sie erbrochen?	1	2	3	4

Bitte wenden

Während der letzten Woche:

	Überhaupt nicht	Wenig	Mäßig	Sehr
16. Hatten Sie Verstopfung?	1	2	3	4
17. Hatten Sie Durchfall?	1	2	3	4
18. Waren Sie müde?	1	2	3	4
19. Fühlten Sie sich durch Schmerzen in Ihrem alltäglichen Leben beeinträchtigt?	1	2	3	4
20. Hatten Sie Schwierigkeiten sich auf etwas zu konzentrieren, z.B. auf das Zeitunglesen oder das Fernsehen?	1	2	3	4
21. Fühlten Sie sich angespannt?	1	2	3	4
22. Haben Sie sich Sorgen gemacht?	1	2	3	4
23. Waren Sie reizbar?	1	2	3	4
24. Fühlten Sie sich niedergeschlagen?	1	2	3	4
25. Hatten Sie Schwierigkeiten, sich an Dinge zu erinnern?	1	2	3	4
26. Hat Ihr körperlicher Zustand oder Ihre medizinische Behandlung Ihr Familienleben beeinträchtigt?	1	2	3	4
27. Hat Ihr körperlicher Zustand oder Ihre medizinische Behandlung Ihr Zusammensein oder Ihre gemeinsamen Unternehmungen mit anderen Menschen beeinträchtigt?	1	2	3	4
28. Hat Ihr körperlicher Zustand oder Ihre medizinische Behandlung für Sie finanzielle Schwierigkeiten mit sich gebracht?	1	2	3	4

Bitte kreuzen Sie bei den folgenden Fragen die Zahl zwischen 1 und 7 an, die am besten auf Sie zutrifft

29. Wie würden Sie insgesamt Ihren Gesundheitszustand während der letzten Woche einschätzen?

1	2	3	4	5	6	7
sehr schlecht						ausgezeichnet

30. Wie würden Sie insgesamt Ihre Lebensqualität während der letzten Woche einschätzen?

1	2	3	4	5	6	7
sehr schlecht						ausgezeichnet

EORTC QLQ - BLM30

Patienten klagen oft über die folgenden Symptome und Probleme. Geben Sie bitte an, in welchem Umfang diese Symptome und Probleme während der letzten Woche bei Ihnen aufgetreten sind. Markieren Sie bitte die Zahl, die Ihrem Fall am ehesten entspricht.

BITTE BEANTWORTEN SIE FRAGE 31 - 37 NUR, WENN SIE NICHT UNTER EINER UROSTOMIE LEIDEN

Während der letzten Woche:	**Überhaupt nicht**	**Wenig**	**Mäßig**	**Sehr**
31. Mussten Sie **tagsüber** häufig urinieren?	1	2	3	4
32. Mussten Sie **nachts** häufig urinieren?	1	2	3	4
33. Mussten Sie sich beeilen, zur Toilette zu kommen, sobald Sie Harndrang verspürten?	1	2	3	4
34. War es schwer für Sie, genügend Schlaf zu bekommen, weil Sie nachts oft aufstehen mussten, um zu urinieren?	1	2	3	4
35. War es schwierig für Sie, das Haus zu verlassen, weil Sie immer in der Nähe einer Toilette sein wollten?	1	2	3	4
36. Kam es bei Ihnen zu unkontrolliertem Austreten von Harn?	1	2	3	4
37. Spürten Sie ein Brennen oder Schmerzen beim Wasserlassen?	1	2	3	4

BITTE BEANTWORTEN SIE FRAGE 38 - 43 NUR, WENN SIE UNTER EINER UROSTOMIE LEIDEN

Während der letzten Woche:	**Überhaupt nicht**	**Wenig**	**Mäßig**	**Sehr**
38. Ist Urin aus dem Urostomiebeutel ausgetreten?	1	2	3	4
39. War die Pflege der Urostomie schwierig?	1	2	3	4
40. Litten Sie unter Hautreizungen im Bereich der Urostomie?	1	2	3	4
41. War Ihnen die Urostomie peinlich?	1	2	3	4
42. Waren Sie bei der Pflege der Urostomie von anderen abhängig?	1	2	3	4
43. Mussten Sie den Urostomiebeutel häufig wechseln?	1	2	3	4

BITTE BEANTWORTEN SIE FRAGE 44 NUR, WENN SIE IM VERLAUF DER LETZTEN WOCHE EINEN KATHETER VERWENDET HABEN

44. Hatten Sie Probleme mit der Selbstkatheterisierung? (Einführen eines Schlauches in die Blase, um Urin abzulassen)	1	2	3	4

Bitte blättern Sie um.

Während der letzten Woche:

	Überhaupt nicht	Wenig	Mäßig	Sehr
45. Waren Sie wegen Ihres zukünftigen Gesundheitszustandes besorgt?	1	2	3	4
46. Haben Sie sich Sorgen wegen der Ergebnisse von Untersuchungen und Tests gemacht?	1	2	3	4
47. Haben Sie sich Sorgen über eventuelle spätere Behandlungen gemacht?	1	2	3	4
48. Fühlte sich Ihr Bauch aufgebläht an?	1	2	3	4
49. Hatten Sie Blähungen?	1	2	3	4
50. Fühlten Sie sich weniger attraktiv aufgrund Ihrer Krankheit oder Behandlung?	1	2	3	4
51. Waren Sie mit Ihrem Körper unzufrieden?	1	2	3	4
52 Fühlten Sie sich aufgrund Ihrer Krankheit oder Behandlung weniger als Frau / als Mann?	1	2	3	4

In den vergangenen 4 Wochen:

	Überhaupt nicht	Wenig	Mäßig	Sehr
53. Wie stark waren Sie an Sex interessiert?	1	2	3	4
54. In welchem Ausmass waren Sie sexuell aktiv (mit oder ohne Geschlechtsverkehr)?	1	2	3	4
55. **Nur für Männer:** Hatten Sie Schwierigkeiten, eine Erektion zu bekommen oder aufrechtzuerhalten?	1	2	3	4
56. **Nur für Männer:** Hatten Sie Ejakulationsprobleme (z. B. trockene Ejakulation)?	1	2	3	4

Bitte beantworten Sie die folgenden 4 Fragen nur, wenn Sie in den vergangenen 4 Wochen sexuell aktiv waren:	Überhaupt nicht	Wenig	Mäßig	Sehr
57. Hatten Sie ein ungutes Gefühl, weil Sie sexuell intim waren?	1	2	3	4
58. Waren Sie beunruhigt darüber, dass Sie Ihren Partner beim Geschlechtsverkehr wegen Ihrer Blasenbehandlung anstecken könnten?	1	2	3	4
59. In welchem Ausmass haben Sie den Sex genossen?	1	2	3	4
60. **Nur für Frauen:** Hatten Sie beim Geschlechtsverkehr eine trockene Scheide oder andere Probleme?	1	2	3	4

SF-36

1. **In der Regel würden Sie sagen, Ihre Gesundheit ist:**

   a) Gut (1)
   b) Sehr gut (2)
   c) Gut (3)
   d) Mäßig (4)
   e) Mangelhaft (5)

2. **Im Vergleich zu vor einem Jahr, wie würden Sie Ihrem Gesundheit im Allgemeinen jetzt beurteilen?**

a) Jetzt viel besser als vor einem Jahr (1)
b) Etwas besser jetzt als vor einem Jahr (2)
c) Ungefähr die gleiche (3)
d) Etwas schlechter als vor einem Jahr (4)
e) Viel schlimmer als vor einem Jahr (5)

Die folgenden Punkte handeln von Aktivitäten, die Sie während eines typischen Tages tun könnten. Begrenzt Sie Ihre Gesundheit bei der Ausübung dieser Aktivitäten? Wenn ja, wie viel?

3. **Kräftige Aktivitäten, wie Laufen, Heben schwerer Objekte, die Teilnahme an anstrengenden Sport**

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

4. **Mäßige Aktivitäten, wie das Verschieben eines Tisch und das Schieben eines Staubsaugers, Bowling oder Golf spielen**

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

5. **Heben oder Tragen von Lebensmitteln**

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

6. **Treppensteigen (mehrere Stockwerke)**

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

7. Treppensteigen (ein Stockwerk)

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

8. Sich biegen, knien, oder sich bücken

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

9. Gehen mehr als eine Meile (ca. 1.7km)

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

10. Gehen um mehrere Wohnblöcke

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

11. Gehen um <u>einen einzigen</u> einem Block

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

12. Baden oder sich selbst Anziehen

a) Ja, starke Einschränkung (1)
b) Ja, aber nur geringe Einschränkung (2)
c) Nein, überhaupt nicht eingeschränkt (3)

In den letzten 4 Wochen hatten Sie eine der folgenden Schwierigkeiten bei Ihrer Arbeit oder anderen alltäglichen Tätigkeiten als Ergebnis Ihrer körperlichen Gesundheit?

13. Sie haben die Menge der Zeit reduziert, die Sie für Ihre Arbeit oder andere Aktivitäten verbracht haben

a) Ja
b) Nein

14. Sie haben weniger erzielt als Sie erreichen wollten

a) Ja
b) Nein

15. Sie waren in der Art der Arbeit oder anderen Tätigkeiten beschränkt

a) Ja
b) Nein

16. Sie hatten Schwierigkeiten bei der Ausführung der Arbeit oder anderen Tätigkeiten (zum Beispiel war es mit einem zusätzlichen Aufwand verbunden)

a) Ja
b) Nein

Während der letzten 4 Wochen hatten Sie eine der folgenden Schwierigkeiten bei Ihrer Arbeit oder anderen alltäglichen Tätigkeiten als Folge von emotionalen Problemen (wie z. B. deprimiert oder ängstlich sein)?

17. Sie haben die Menge der Zeit reduziert, die Sie für Ihre Arbeit oder andere Aktivitäten verbracht haben

a) JA
b) Nein

18. Sie haben weniger erzielt als Sie erreichen wollten

a) JA
b) Nein

19. Sie hatten Schwierigkeiten bei der Ausführung der Arbeit oder anderen Tätigkeiten (zum Beispiel war es mit einem zusätzlichen Aufwand verbunden)

a) JA
b) Nein

20. In den letzten 4 Wochen, in welchem Umfang hat Ihre körperliche Gesundheit oder emotionale Probleme ihre üblichen normalen sozialen Aktivitäten mit Familie, Freunden, Nachbarn oder Gruppen beeinträchtigt?

a) Überhaupt nicht (1)
b) Leicht (2)
c) Mäßig (3)
d) Ganz ein bisschen (4)
e) Extrem (5)

21. Wie ausgeprägt waren ihre körperliche Schmerzen während der letzten 4 Wochen?

a) Keine (1)
b) Ganz leicht (2)
c) Leicht (3)
d) Mäßig (4)
e) Stark (5)
f) Sehr stark (6)

22. Wie stark haben in den letzten 4 Wochen ihre Schmerz Sie bei der Ausübung Ihrer normalen Arbeit (einschließlich der Arbeit außerhalb des Hauses und Hausarbeit) beeinträchtigt?

a) Überhaupt nicht (1)
b) Leicht (2)
c) Mäßig (3)
d) Ziemlich stark (4)
e) Extrem (5)

Diese Fragen handeln darüber, wie Sie sich in den letzten 4 Wochen fühlen und wie es um Sie stand. Für jede Frage, kreuzen Sie bitte nur eine Antwort an, die die Art und Weise wie Sie sich gefühlt haben, am genauesten wiedergibt.

23. Hatten Sie das Gefühl voller Elan zu sein?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Ein gutes Stück während dieser Zeit (3)
d) Etwas während dieser Zeit (4)
e) Ein wenig während dieser Zeit (5)
f) Nicht während dieser Zeit (6)

24. Waren Sie sehr nervös?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Ein gutes Stück von der Zeit (3)
d) Etwas während dieser Zeit (4)
e) Ein wenig während dieser Zeit (5)
f) Nicht während dieser Zeit (6)

25. Haben Sie sich so niedergeschlagen gefühlt, dass Sie nichts aufheitern konnte?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Ein gutes Stück von der Zeit (3)

d) Etwas während dieser Zeit (4)
e) Ein wenig während dieser Zeit (5)
f) Nicht während dieser Zeit (6)

26.Haben Sie ruhig und gelassen gefühlt?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Ein gutes Stück von der Zeit (3)
d) Etwas während dieser Zeit (4)
e) Ein wenig während dieser Zeit (5)
f) Nicht während dieser Zeit (6)

27.Hatten Sie viel Energie?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Ein gutes Stück von der Zeit (3)
d) Etwas während dieser Zeit (4)
e) Ein wenig während dieser Zeit (5)
f) Nicht während dieser Zeit (6)

28.Fühlten Sie sich niedergeschlagen und deprimiert?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Ein gutes Stück von der Zeit (3)
d) Etwas während dieser Zeit (4)
e) Ein wenig während dieser Zeit (5)
f) Nicht während dieser Zeit (6)

29.Fühlten Sie sich erschöpft?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Ein gutes Stück von der Zeit (3)
d) Etwas während dieser Zeit (4)
e) Ein wenig während dieser Zeit (5)
f) Nicht während dieser Zeit (6)

30. Haben Sie sich glücklicher gefühlt?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Ein gutes Stück von der Zeit (3)
d) Etwas während dieser Zeit (4)
e) Ein wenig während dieser Zeit (5)
f) Nicht während dieser Zeit (6)

31.Fühlten Sie sich müde?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Ein gutes Stück von der Zeit (3)
d) Etwas während dieser Zeit (4)
e) Ein wenig während dieser Zeit (5)
f) Nicht während dieser Zeit (6)

32. In den letzten 4 Wochen, wie viel Zeit haben sich Ihre körperliche Gesundheit oder emotionale Probleme mit Ihrem sozialen Aktivitäten (z.B. Besuche bei Freunden, Verwandten, etc.) beeinträchtigt?

a) Die ganze Zeit (1)
b) Die meiste Zeit (2)
c) Einiges währen dieser Zeit (3)
d) Ein wenig während dieser Zeit (4)

Wie richtig oder falsch ist jede der folgenden Aussagen für Sie?

33. Ich glaube, dass ich leichter krank werde als andere Menschen.

a) Stimmt definitiv (1)
b) Stimmt meistens (2)
c) Sie wissen nicht (3)
d) Stimmt meistens nicht (4)
e) Stimmt definitiv nicht (5)

34. Ich bin so gesund wie jeder den ich kenne.

a) Stimmt definitiv (1)
b) Stimmt meistens (2)
c) Sie wissen nicht (3)
d) Stimmt meistens nicht (4)
e) Stimmt definitiv nicht (5)

35. Ich erwarte, dass sich mein gesundheitlicher Zustand noch verschlechtern wird.

a) Stimmt definitiv (1)
b) Stimmt meistens (2)
c) Sie wissen nicht (3)
d) Stimmt meistens nicht (4)
e) Stimmt definitiv nicht (5)

36. Meine Gesundheit ist hervorragend.

a) Stimmt definitiv (1)
b) Stimmt meistens (2)
c) Sie wissen nicht (3)
d) Stimmt meistens nicht (4)
e) Stimmt definitiv nicht (5)

Sehr geehrte(r) Patient(in),

für die folgenden Fragen möchten wir Sie bitten, sie so zu beantworten, wie Sie sich **damals unmittelbar 2 Wochen vor der grossen Blasenoperation (radikale Zystektomie)** von Seiten ihrer Stuhlgangsgewohnheiten gefühlt haben.

Q1. Wie oft in den letzten 2 Wochen fühlten Sie sich durch die Häufigkeit des Stuhlganges belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

Q2. Wie oft in den letzten 2 Wochen fühlten Sie sich durch die dranghaftliche Stuhlbewegungen belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

Q3. Wie oft in den letzten 2 Wochen fühlten Sie sich durch einen Durchfall belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

Q4. Wie oft in den letzten 2 Wochen fühlten Sie sich durch Verstopfung belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

Q5. Wie oft in den letzten 2 Wochen fühlten Sie sich durch unkontrollierten Stuhlgangsverlust (Stuhlinkontinenz) belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

Sehr geehrte(r) Patient(in),

für die folgenden Fragen möchten wir Sie bitten, sie so zu beantworten, wie Sie sich **in den letzten 2 Wochen** von Seiten ihrer Stuhlgangsgewohnheiten gefühlt haben.

Q1. Wie oft in den letzten 2 Wochen fühlten Sie sich durch die Häufigkeit des Stuhlganges belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

Q2. Wie oft in den letzten 2 Wochen fühlten Sie sich durch die dranghaftliche Stuhlbewegungen belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

Q3. Wie oft in den letzten 2 Wochen fühlten Sie sich durch einen Durchfall belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

Q4. Wie oft in den letzten 2 Wochen fühlten Sie sich durch Verstopfung belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

Q5. Wie oft in den letzten 2 Wochen fühlten Sie sich durch unkontrollierten Stuhlgangsverlust (Stuhlinkontinenz) belästigt?
Die ganze Zeit (0), die meiste Zeit (1), manchmal (2), selten (3), nie (4)

SPEZIFISCHER FRAGEBOGEN FÜR PATIENTEN MIT NEOBLASE

1. **Nehmen Sie Vitamin B12 Präparate ein?**
   a) Ja
   b) Nein
2. **Nehmen Sie Natrium-Bikarbonat (Na HCO3) ein (z.B. Bicanorm®, Nephrotrans ®)?**
   a) Ja
   b) Nein
3. **Wie viele Harnwegsinfektionen hatten Sie im letzten Jahr?**
   A) 1 B) 2 C) 3 D) 4 E) > 4
4. **Wenn ja, waren diese Harnwegsinfektionen fieberhaft?**
   a) Ja
   b) Nein
5. **Wie viel ml Liter urinieren Sie im Durchschnitt ungefähr (grober Schätzwert)?**
   A) <100 ml
   B) 100-200 ml
   C) 200-300 ml
   D) 300-400 ml
   E) 400-500 ml
   F) >500 ml

6. **Müssen Sie beim Wasserlassen die Bauchpresse betätigen, damit die Neoblase entleert werden kann?**
   A) ja B) Nein
7. **Benutzen Sie Katheter um die Blase zu entleeren?**
   A) ja B) Nein
8. **Wenn ja, wie oft pro 24 Studen führen Sie einen Einmalkatheterismus durch?**
   Anzahl tagsüber:……. Anzahl nachts:……
   Kathetervolumen tagsüber:……. Kathetervolumen nachts:……

9. Verspüren Sie Schmerzen über den Nieren während des Wasserlassens?

A) ja B) Nein

10. Benutzen Sie Vorlagen?

Tagsüber

A) Ja B) Nein

Wenn Ja, wie viele?

…….

Sind Vorlagen tagsüber feucht oder naß?

A) feucht B) naß

Verwenden Sie die Vorlage(n) lediglich als „Sicherheitsvorlage“?

A) Ja B) Nein

Angenommen es kommt zum Urinverlust in die Vorlage tagsüber. Wenn Sie nun Ihre Vorlage wiegen, um wie viel Gramm ist diese hiernach schwerer? (Gewicht feuchte/nasse Vorlage minus Gewicht trockene Vorlage)

……..g

Nachts

A) Ja B) Nein

Wenn Ja, wie viele?

…….

Sind die Vorlagen nachts feucht oder naß?

A) feucht B) naß

Verwenden Sie die Vorlage(n) lediglich als „Sicherheitsvorlage“?

A) Ja B) Nein

Angenommen es kommt zum Urinverlust in die Vorlage nachts. Wenn Sie nun Ihre Vorlage wiegen, um wie viel Gramm ist diese hiernach schwerer?
(Gewicht feuchte/nasse Vorlage minus Gewicht trockene Vorlage)
……..g

11. Für männliche Patienten: Benutzen Sie eine Kondomurinal?

A) Ja B) Nein

12. Merken Sie, dass sich in der Neoblase Schleim bildet?

A) Ja B) Nein C) Bin mir nicht sicher

13. Bei Männern: Haben Sie vor der radikalen Zystektomie Präparate zur Steigerung der erektile Funktion (Gliedsteife) eingenommen (z.B. Viagra ®, Cialis ®, Levitra ®)?

A) Ja B) Nein

14. Bei Männern: Nehmen Sie derzeit Präparate zur Steigerung der erektile Funktion (Gliedsteife) ein (z.B. Viagra ®, Cialis ®, Levitra ®) ?

A) Ja B) Nein