OBJECTIVES: The aim of this report is to present our 30 years experience with various types of urinary diversions, in particular the Bricker and Studer techniques for the management of muscle invasive bladder cancer at our institution. Perioperative, early and late complications are also evaluated. MATERIAL AND METHODS: Between 1977 and 2007, 186 male and 15 female patients underwent combined radical cystectomy, pelvic lymphadenectomy and urinary diversion. In two subgroups of patients we evaluated the complications, divided as early and late, and subdivided as those related or unrelated to the neobladder. Mean follow up time was 28 months (range 12-60 months). RESULTS: Two main types of urinary diversion were performed: the ileal conduit diversion using a technique previously described by Bricker and the ileal neobladder diversion using a technique previously described by a Studer. The ages at surgery ranged from 40 to 82 years with a mean age of 60 years. Histopathologically, transitional cell carcinoma was the most common tumor cell type (93.7%), followed by diffuse papilomatosis (5.5%) and adenocarcinoma (0.7%). The pathological tumor stage was pT1 (4.7%), pT2 (31.4%), pT3 (50.3%) and pT4a (13.3%). Histological evidence of regional lymph node involvement was seen in 25% of the cases. From 52 patients from the Studer subgroup perioperative complications were found in 16 patients (30.7%). Specific early complications directly related to the neobladder occurred in 14 (26.9%) patients. Prolonged ileus in 2 patient (3.8%), ureteral leakage in 9 patients (17.3%), mucous buildup within the diversion in 3 patients (5.7%). Late complications occurred in 10 patients (19.2%): retention of the urine in 4 patients (7.6%) (stricture of the urethra-pouch anastomosis in one 1 patient) and to big reservoir in 3 patients. One patient (1.9%) developed prolonged metabolic acidosis. Stone formation was observed in one patient, two years postoperatively. Unilateral hydronephrosis was observed in 2 patients whereas bilateral hydronephrosis was observed in one patients at one year postoperatively. Perioperative and late complications were similar in the 32 patients from the Bricker subgroup. CONCLUSION: We show that our results with urinary diversion are promising in patients requiring radical cystoprostatectomy. The two methods preferred in our institution offer a sufficient protection of the upper urinary tract with a low complication rate, good voiding function and continence.

Key words: urinary diversion, cystoprostatectomy, invasive bladder cancer

INTRODUCTION

Urinary diversion has a history of nearly 150 years, and the ileal conduit previously described by Bricker has long been considered the gold standard for urinary diversion. Orthotopic substitution of the bladder following cystectomy is currently well established. It provides the patient with a superior cosmetic appearance, and the potential for normal voiding function and continence. Despite these advantages, this type of diversion tends to be reserved for selected patients due in part to the perception that the greater technical complexity of orthotopic urinary diversion leads to greater perioperative and long-term morbidity. This procedure, which requires a bowel segment, avoids an abdominal stoma and may offer an improved quality of life for patients undergoing radical cystectomy for bladder cancer. In 1989, Studer et al. described low-pressure bladder substitution using a spherical reservoir consisting of four cross-folded ileal detubularized segments. This neobladder uses an afferent isoperistaltic ileal segment with direct ureteroneal anastomosis, which functions as an antireflex mechanism in order to protect the upper urinary tract. Since 1997, we have adopted the Studer orthotopic bladder substitution following radical cystectomy in 63 male patients with invasive bladder cancer. In the present study, we report our 30
years experience with various types of urinary diversions, in particular the Bricker and Studer techniques for the management of muscle invasive bladder cancer at our Clinic. Perioperative, early and late complications are also evaluated.

PATIENTS AND METHODS

Patients Between 1977. and 2007., 186 male and 15 female patients underwent combined radical cystectomy and pelvic lymphadenectomy. Charts of only 127 patients had complete information and constituted the material of the current study. Two main types of urinary diversion were performed subsequently. The ileal conduit diversion using a technique previously described by Bricker and the ileal neobladder diversion using a technique previously described by a Studer. In addition, although rarely, in yearly 80’s we performed 5 uretercutanostomas and several urinary derivations using a technique previously described by Coffy. Bladder cancer was diagnosed by cystoscopic and bimanual examination plus random biopsy. Preoperative staging work-up involved complete history and physical examination, complete laboratory work-up, chest radiography, excretory urography and computerized tomography of the abdomen and pelvis (for patients with high grade and muscle invasive tumors). The indication for cystectomy was based on cystoscopic and biopsy findings, including tumor invasion of the muscularis propria or prostatic stroma without evidence of metastasis; high-grade, invasive tumors associated with carcinoma in situ (CIS); CIS refractory to intravesical chemotherapy or immunotherapy; recurrent multifocal superficial disease refractory to repeated transurethral resection (papilotomatosis) with/without intravesical therapy and tumors involving a bladder diverticulum. All patients underwent bilateral pelvic iliac lymphadenectomy with en bloc radical cystectomy and urinary diversion. Of note, in our series we have performed standard pelvic lymph node monoblock dissection that involves obturator packets and extends laterally to the external iliac and hypogastric vessels. The cephalad extent of the dissection terminates at the bifurcation of the common iliac vessels. An extended version of this procedure, preferred by some surgeons from our Clinic, which demarcates the inferior mesenteric artery as the cephalad boundary and includes paracaval, intra-aortocaval, para-aortic, presacral, common iliac, and external iliac nodes as part of the dissection was done very rarely. Concomitant urethrectomy was performed only in patients with tumors involving bladder neck, prostatic urethra or diffuse CIS. All the cystectomy specimens were pathologically examined according to the same protocol. Following cystectomy, patients were initially seen one month after surgery and then every 3 months for 1 year and every 6 months until disease progression or death. Patients were followed-up by complete physical examination, complete renal profile and blood picture, chest X-ray, CT abdomen and pelvis and isotopic bone scan whenever indicated. However we have to acknowledge that due to the separation of Yugoslav federation in 1991., an important number of our patients were lost during follow up. That is the reason why we have analyzed a limited number of patients divided in two main subgroups. In a subgroup of 32 patients from the Bricker group (operated between 1986-1991.) and 52 from the Studer group (operated from 1997. until 2001.), we evaluated early post-operative and late complications. The mean follow-up period for both groups was 28 months (range 12-60 months). The patients were followed at regular intervals of 3 months for the first year and at least once a year thereafter. An upper tract study (excretory urogram or computerized tomography (CT) is obtained at 3 months postoperatively to assess surgical anatomy, and CT with
intravenous contrast medium is performed every 6 months for the first 2 years to assess the upper tracts and reservoir, and to search for recurrent tumor. After 2 years CT is performed annually until year 5 and thereafter when indicated. Of 52 patients from the Studer group, 31 were followed for more than 3 years.

The study of functional outcome was focused on 31 patients who remained cancer free and were available for complete follow-up for at least 3 years after the surgery. Complications were defined as perioperative if they occurred within 30 days after the operation and late if they occurred later than 30 days. Lower urinary tract function and urinary continence by post-void ultrasound of the reservoir to assess neobladder empting; urodynamic studies including uroflowmetry was also performed. Continence was strictly assessed and rated as excellent if the patient was completely dry at all times, good if there were occasional or sporadic episodes of leakage but no need for protection, fair if no more than a single pad was required within 24 h and unsatisfactory if more than 1 pad were required within 24 h. The status of the upper urinary tract was assessed by radiological assessment using intravenous pyeloureterography (IVP), and renal function with the metabolic status was also monitored by serum urea nitrogen and creatinine with serum chloride and arterial HCO3.

Surgical Techniques

The ileal conduit diversion was performed using the technique previously described by Bricker1. A 15 cm. segment of ileum was isolated, and stented Bricker ureterointestinal anastomoses were performed. This segment was then brought through the abdominal wall and a rosebud stoma was matured. The technique of the ileal bladder substitution has been described by Studer et al. 3,5. Briefly, an ileal segment 60 cm in length was isolated 25 cm proximal to the ileocecal valve. The distal end of the ileal segment, 40-45 cm in length, was opened along its antimesenteric border. The construction of the reservoir was performed as previously described by Studer (REF). Ureterointestinal anastomoses were performed in an open end-to-side fashion at the proximal part of the ileal segment. A hole with a diameter of 5 mm was cut out of the pouch wall and four 2-0 polyglycolic acid seromuscular sutures were placed between the hole in the reservoir and the edge of the membranous urethra and a 18F silicone urethral catheter was inserted before tying the four sutures at 10, 2, 5 and 7 o’clock positions of the membranous urethra. On the 7th to 10th postoperative days, the ureteric stents were removed. After excluding fistula formation of the reservoir and leakage from the pouch-urethral anastomosis by "cystogram" on the 14th day, the urethral catheter was removed and the patients’ were instructed how to void.

POSTOPERATIVE CARE

The pouch is flushed with 40 cc normal saline every 12 hours and mucous clots are aspirated. Patients are initially instructed to void while sitting, and to relax the pelvic floor and expel the urine by Valsalva’s maneuver. The capacity of the neobladder gradually increases as the voiding interval is lengthened to 4 to 6 hours. Creatinine, bicarbonate and serum electrolytes are monitored postoperatively and every 3 months thereafter. Serum vitamin B12 is measured at 1 month and annually.

STATISTICAL ANALYSIS

Values are expressed as means plus or minus standard deviation (SD). Differences between means for the various group in the study were compared using the Student’s t-test for independent population means and considered statistically significant when the P-values were %.
RESULTS

General characteristics

Most of the urinary derivations were performed in our Clinic in the last decade (127 patients) whereas 36 and 27 urinary diversions were performed form 1986.-1997. and from 1977. to 1986., respectfully (Figure 1). Charts of only 127 patients from the last 10 years had complete information and constituted the material of the current study. Figure 2 shows a 10 year distribution of the two main types of urinary derivations performed in our Clinic. The ages at surgery ranged from 40 to 82 years with a mean age of 60 years. Mean operative time for cystectomy, lymphadenectomy and ileal conduit diversion was 6 hours 45 minutes (range 5 hours 30 minutes to 9 hours 30 minutes, whereas for Studer neobladder was 7 hours 45 minutes (range 6 hours to 11 hours). The mean blood loss was 1200 ml (SD: 671 ml). Mean hospital stay was 41 days for the Bricker (from 11 to 65) group and 46 for the Studer group (from 21 to 70) and it is statistically significant (p<0.001). Interestingly, when analyzing by year of operation, we observe a significant decrease of the mean hospital stay with every year passed reaching a mean of 21 and 17 days for the last year for the Studer and Bricker procedure respectively (Figure 3). The same was thru for mean operating time (Figure 4). The substantial long operative time observed is due to several complicated cases mostly in our earlier experience with Studer ileal neobladder, when we encountered the problem of short mesentery in four patients. In addition, one patient from the Bricker group had pemphigus vulgaris and developed pulmonary complications postoperatively. Histopathologically, TCC was the most common tumor cell type diagnosed in 119 patients (93.7%), followed by diffuse papilomatosis in 7 patients (5.5%) and adenocarcinoma in one patients (0.7%). The pathological tumor stage was pT1 or less in 6 patients (4.7%), pT2 in 40 patients (31.4%), pT3 in 64 patients (50.3 %) and pT4a in 17 patients (13.3%). Tumor grade was 1, 2 and 3 in 5 patients (3.9%), 47 patients (37%) and 75 patients (59.1%), respectively.

Lymphnodes evaluation

For all of our patients in our series we have performed standard pelvic lymph node dissection. However, we have analyzed precisely only the Bricker subgroup. Histologically evident of regional lymph node involvement was seen in 25% of the cases from which 37% were found to be microscopic. The pathological tumor stage associated with lymph nodes metastasis was as follows: 25% of the patients who had metastasis were in stage T2 whereas 75% of the patients were in T3 stage. Concerning the grade of the tumor, 25% of the patients with lymph node metastasis were G2 whereas 75% were in G3. Most of metastasis were found in fossa iliaca externa (87.5%), fossa obturatoria (50%) and fossa hypogastrica in 37.5% of the cases. Regarding the location of the tumor in the bladder in patients with positive locoregional lymph nodes we found that in 62.5% of the cases the tumor was located on the trigonum, 25% in the bladder neck and 12.5% laterally. The accuracy of lymphography, lymphoscintigraphy and CT preoperatively in clinical staging of positive lymph nodes was 59%, 56% and 63%, respectively.

Perioperative and Late Complications

In the subgroups of 52 patients that were followed for early and late complications from the Studer group, there was one perioperative death due to damaged rectum. Perioperative complications were found in 16 patients (30.7%). Three patients (5.7%) had neobladder-unrelated and general early complications that can be expected from any major pelvic operation, including 2 wound infections and one pulmonary embolism. The former 2 patients required ultrasound-guided drainage of the abscess. Specific early complications directly related to the neobladder occurred in 14 (26.9%) patients. Prolonged ileus in 2 patient (3.8%), ureteral leakage in 9 patients (17.3%), mucous buildup within the diversion in 3 patients (5.7%). Late complications occurred in 10 patients (19.2%): retention of the urine in 4 patients (7.6%) (stricture of the urethropouch anastomosis in one patient) and to big reservoir in 3 patients. In this former, stricture of the urethral anastomosis was treated by transurethral incision of the urethra-pouch junction. One patient (1.9 %) developed prolonged metabolic acidosis. Stone formation was observed in one patient, two years postoperatively. Perioperative and late complications were similar in the 32 patients from the Bricker subgroup including: 2 revised patient due to wound dehiscence (6.2%), 1 patient with acute pyelonephritis (3.1%) whereas prolonged ileus was found in 3 patients (9.3%). Urinary leakage from ureteroenteric anastomosis was observed in 3 patients (9.3%). Prolonged lymphoarea (average 16 days) was observed in 4 patients (12.5%). Late complications included: obstruction in the ureteroenteric anastomosis in 2 patients (6.2%), bowel obstruction in 4 patients (12.5%) and transient paraplegia inferior in one patient (3.1%) treated successfully with corticosteroids.

Functional Outcome and continence

All patients from the Studer group were able to void urine, first in a sitting position and later in an upright position. Despite a small capacity in early postoperative period, the capacity increased gradually with time, reaching almost 250 ml and over 300 ml at 6 months and 1 year after the surgery, respectively, and was maintained almost constant thereafter. There was 25 continent patients after 6 months, residual urine: 80 ml (30-220), capacity: 420 ml (250-660), MFR: 11 ml/sec (5-20 ml/sec), average flow: 7 ml/sec, first sensation to void: 300 ml (220-350), peak pressure: 26 cm/water (13-45). There were also no significant differences of these parameters of the urodynamic study such as the maximum flow rate, average flow rate and pressure of maximum capacity in the postoperative periods. In a small subgroup of 20 patients from Studer group we analyzed urinary continence. At 1 postoperatively, 11 patients achieved had excellent or good conti-
nence and required no pad during the day (65%) and 8 of them had satisfactory control during nighttime and only one patient had nocturnal incontinence requiring a single pad to avoid leakage.

**Upper Urinary Tract Status**

Among all patients from the Studer group, unilateral hydroureteronephrosis was observed in only 2 patients (2 re-noureteral units) whereas bilateral hydroureteronephrosis was observed in one patients at one year postoperatively. Meanwhile the remaining 99 renoureteral units did not show any ectasia or obstruction during the entire IVP examination at 1 year after the surgery. During follow-up, none of the patients demonstrated significant changes in serum urea nitrogen, creatinine and chloride levels.

**DISCUSSION**

During the last decade, radical cystectomy with pelvic lymphadenectomy has been established as the gold standard for treatment of invasive bladder cancer. It effectively removes the primary tumor and the regional lymph nodes that may contain metastases in about 25% of patients undergoing this procedure. However, even if muscle-invasive bladder cancer was shown to be organ confined before radical cystectomy, up to one half of patients ultimately die of disease in spite of apparently complete surgical removal. This point out the aggressive nature of this disease with early metastatic spread, but also the need for early additional therapy in some patients to eliminate potential micrometastasis. According to the treatment EAU guidelines, patients with non-metastatic, operable, invasive bladder cancer are treated with radical cystectomy, pelvic lymphadenectomy and urinary diversion. Orthotopic neobladder after radical cystectomy offers quality of life advantages over an ileal conduit for patients who want to avoid an abdominal stoma. However, even if muscle-invasive bladder cancer was shown to be organ confined before radical cystectomy, up to one half of patients ultimately die of disease in spite of apparently complete surgical removal. This point out the aggressive nature of this disease with early metastatic spread, but also the need for early additional therapy in some patients to eliminate potential micrometastasis. According to the treatment EAU guidelines, patients with non-metastatic, operable, invasive bladder cancer are treated with radical cystectomy, pelvic lymphadenectomy and urinary diversion.

Orthotopic neobladder after radical cystectomy offers quality of life advantages over an ileal conduit for patients who want to avoid an abdominal stoma. The functional voiding outcome with a neobladder is excellent with high continence rates and generally good bladder emptying. Despite these advantages, there is a general perception that creation of a neobladder is a technically complex and lengthy procedure associated with an increase in perioperative morbidity, complications and reoperative rates. Elderly patients as well as high risk patients with significant medical co-morbidities are often not offered a neobladder. To the contrary, Benson et al recently reported no difference in complication rates of patients undergoing ileal conduit versus orthotopic right colon, hemi-Kock or sigmoid neobladder diversion. Similarly, Gibure et al reported comparable perioperative and long-term morbidity rates for the ileal conduit and Studer neobladder. In the present report the perioperative and long-term morbidity the 2 techniques was similar as well. The requirements for an ideal intestinal bladder substitution are low pressure, adequate capacity and high compliance, which provide continence and voluntary control of voiding without residual urine. It is obvious that these factors facilitate a higher quality of life following orthotopic bladder substitution. The Studer orthotopic ileal neobladder has the advantages of satisfactory continence rate, absence of urinary leakage and freedom from intermittent catheterization. In addition, renal function is preserved, and intestinal malabsorption and fluid and electrolyte imbalances are avoided. These features have rendered the Studer bladder substitution one of the most ideal orthotopic urinary diversions. Of note, orthotopic bladder replacement stimulates earlier cystectomy at a time when the potential for cure is highest. In addition, our experience with orthotopic bladder substitution shows that patients who are well motivated and carefully selected can achieve an outstanding outcome. For these patients life is similar to that with a native lower urinary tract. However, enthusiasm for orthotopic reconstruction should be tempered by an understanding of its indications and how not to contravene them.

In the present study, we also focused on the complication rate, functional outcome, continence rate and renal function level with the metabolic status. The early and late complication rates in our series were 25 and 18.73%, respectively. These results are only a bit higher as compared with those of previously reported series, in which the perioperative complication rate ranged from 9 to 18% and the late complication rate ranged from 6 to 24%. Furthermore, there was no remarkable difference in types of complications between our cases and previously reported series. The main mechanism for urinary control following radical cystectomy with orthotopic bladder substitution seems to be the same as that after radical prostatectomy, that is preservation of the periurethral sphincter mechanism and muscles of the pelvic floor. However, Parekh et al reported that patients with the bladder substitution achieve daytime control more rapidly than those undergoing radical prostatectomy, and stress urinary incontinence is rarely an issue. The intestinal neobladder has no detrusor sphincteric reflux that increases urethral closure pressure as bladder pressure increases. Also, unlike a normal bladder, there are no vesical sensory fibers allowing feedback to the brain to alert the patient when the reservoir is full, particularly at night.

Clinical staging of lymph node status in patients with muscle-invasive disease remains inaccurate. The finding of clinically occult disease can range from 15% to 27% with cross-sectional MRI and CT. In the present study we found 25% of positive lymph nodes (pathohistologically confirmed) after cystectomy which is consistent with other series in the literature. Interestingly, 37% of the positive lymph nodes in our series were found to be microscopic. This suggests that there is a clinical understaging probably due to failure of the radiological methods used in our Institution such as lymphography, lymphoscintigraphy, ultrasonography, CT, MRI. Both clinical stage and lymph node status independently contribute to prediction of prognosis. As shown by our results, the correlation of nodal metastasis with increased clinical stage is clear. New ferromagnetic contrast agents that result in improved staging in patients with prostate cancer may prove valuable in further discrimination of lymph node status among patients with bladder cancer. Current PET techniques are not useful; the reported false-negative rate is approxi-
mately 30%. This is somewhat complicated in the case of muscle-invasive bladder cancer, in that lymphatic drainage of the bladder is variable and minimal data are available to correlate tumor position in the bladder with positive lymph node location. In our series we found that in 62.5% of the cases the tumor was located on the trigonum, 25% in the bladder neck and 12.5% laterally. Additionally, inferential data suggest the phenomena of skip metastases to higher-echelon nodes and of crossing trigonum, 25% in the bladder neck and 12.5% laterally. The role of sentinel nodes, when detected, beyond the obturator node region in a third of cases. This is clearly an area for further study that may yield clinically useful information. In conclusion, we show that our results with urinary diversion are promising in patients requiring radical cystoprostatectomy. The two methods preferred in our institution offer a sufficient protection of the upper urinary tract with a low complication rate, good voiding function and continence.and continence results with two different methods preferred in our Institution.

SUMMARY

URINARNA DERIVACIJA - 30-godišnje iskustvo jednog centra

Cilj ovog rada je da predstavi 30-godišnje iskustvo sa različitim tipovima urinarnih derivacija, posebno sa Bricker-ovom i Studer-ovim tehnikom u lečenju invazivnog karcinozne mokraće bešike u našoj Ustanovi. Perioperativne, rane i kasne komplikacije su takodje evaluirane. Materijal i metod: Izmedju 1977.-2007. godine, 186 muškaraca i 15 žena je podvrgnuto kombinovanoj radikalnoj cistektomiji, pelvičnoj limfadenektomiji i urinarnoj derivaciji. U 2 podgrupe pacijenata evaluirali smo komplikacije koje smo podelili na rane i kasne i one koje imaju ili nemaju uzrok vezan za novoformiranu bešiku. Srednje vreme praćenja bilo je 28 meseci (12-60 meseci). Rezultati: 2 glavna tipa urinarnih derivacija su primjenjeni: ilealni konduit derivacija po Bricker-u i ilealna neobešika po Studer-u. Prosječna starost pacijenata bila je 60 godina (40-82 godine). Histopatološki: tranziciocelularni karcinom je bio najčešći tumor (93,7%), zatim difuzna papilomatoza (5,5%) i adenokarcinom (0,7%). Patološki stadijum tumora bio je pT1 (4,7%), pT2 (31,4%), pT3 (50,3%), pT4a (13,3%). Histološki dokazana zahvaćenost regionalnih limfnih zleza dokazana je u 25% slučajeva. Od 52 pacijenta u grupi gde je radjena Studer-ova operacija perioperativne komplikacije nadjene su u 16 pacijenata (30,7%). Specifične rane komplikacije direktno vezane za neobešiku pojavile su se u 14 bolesnika (26,9%). Ileus se javio kod 2 pacijenta (3,8%), ureteralna fistula u 9 pacijenata (7,3%), zapušenje mukosom kod 3 pacijenta (5,7%). Kasne komplikacije su se pojavile kod 10 pacijenata (19,2%): retencija mokraće kod 4 (7,6%) pacijenata (od čega je kod jednog uzrok bila strikturna na anastomozi izmedju urrete i pauca i veliki rezervoar i dilatacija rezer-voara kod 3 pacijenta ). Kod jed nog pacijenta (1,9%) je došlo do pojave metaboličke acidoze. Formiranje kamena u neobešići je vidjeno kod jednog pacijenta 2 godine posle operacije. Unilateralna ureterohidronefroza je konstatovana kod 2 pacijenta, dok je bilateralna dokazana kod jednog pacijenta godinu dana posle operacije. Perioperativne i kasne komplikacije su bile slične kod 32 bolesnika koji su operisani tehnikom po Bricker-u. Zaključak: Smatramo da su naši rezultati sa urinarnom derivacijom obećavajući kod pacijenata kod kojih je radjena radikalna cistoprostatektomija. Dve metode koje su radjene u našoj Ustanovi nude zadovoljavajući zaštitu gornjih urinarnih puteva sa malim procentom komplikacija i zadovoljavajuću funkcijom mokrenja i kontinencijom.

Ključne reči: urinarna derivacija, cistoprostatektomija, invazivni karcinom bešike

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