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Radical Surgical Treatment of the Urinary Bladder Cancer in Patients Over the Age of 60 – Our Experiences

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ABSTRACT

The goal of the paper was the analysis of patients over the age of 60 suffering from the urinary bladder cancer that underwent radical surgical treatment of the urinary bladder and establishing urine derivation. In the 1972–2008 period 2405 patients with the urinary bladder cancer were treated, 296 (12.3%) of whom underwent radical surgical treatment. The average age was between 60 and 80 years – in 207 (70%) patients. In our patients there were 190 patients (91.6%) with transitional cell cancers. According to TNM classification, T3 stage in 92 (44.4%) patients and T2 stage in 85 (41%) patients were predominant in our study. According to histological criteria, the most common stage was G3 stage – in 151 (73%) patients. Radical cystectomy or combined with urethrectomy was performed in 178 (86%) patients. Unfortunately, in 12% of them (T3 and T4 stages) the inner iliac blood vessels were tied off due to a progressive cancer. The outer supravesical urine derivation (Bricker, U-tubing nephrostomy, and ureterocutaneostomy) was done in 163 (78.7%) patients. The inner derivation (Coffey, ureteroileosigmoidostomy, Mainz-Pouch II) was performed in 17 (8.2%) patients and neovesica (Hautmann, Studer) in 24 (11.5%) patients. There were 74 (35.7%) patients with early postoperative complications. Among them the most dominant were the surgical complications – in 28 (13.5%) patients and distant organ complications – in 22 (10.6%) patients. In 75 (36%) patients with negative nodes the survival rate was 55% after five years. In 73 (35%) patients with positive nodes the survival rate was 27% after five years.

Key words: urinary bladder neoplasm, cystectomy, urinary diversion, incontinent ileostomy

Introduction

Urinary bladder cancer is the most frequent malignant tumour of the urinary tract, mostly occurring between the age 50 and 70. The risk in the urban areas is 50--150 times greater than in the rural areas¹. Some industries are specifically connected with the urinary bladder cancer. They are chemical, paint, varnish, rubber, oil and gas industries². The workers in high risk industries have 30 times greater chances to get the urinary bladder cancer in comparison with other population. Four chemical industry carcinogens were discovered: 4-amino-diphenyl-xenylamine, β -methylamine, benzidine and 4-nitrodiphenyl.

Radical cystectomy is transperitoneal »en block« extirpation of the urinary bladder, prostate and vesicles together with pelvic lymph nodes. As a rule, this operation

includes the extirpation of the uterus, adnexa and the proximal third of the vagina in woman. Nowadays, this surgical intervention is most frequently carried out in case of the invasive urinary bladder tumours. Histological finding of nodes at lymphadenectomy is the only reliable criterion for the assessment of the regional expansion of the disease.

This surgical treatment is closely connected with problem of urinary derivation. Each new method of the urinary derivation has been enthusiastically accepted by urologists during this century as a hope that it will be the perfect form of the urinary bladder substitute. Unfortunately, they became disappointed after some time. Each new method of derivation would be more or less accompanied with the same complications: impossibility of

physiological way of urination, social problems connected with the artificial orifice and later serious complications, with kidneys especially.

Supravesical urinary derivation is called the artificial urinary derivation above the bladder level on the abdomen or into the intestine. It can be performed directly (ureterocutaneostomy), or by the isolated intestinal segment (the ileum or "the colon-conduit"). Bringing the ureter to the intestine can be dual, either with preserved intestinal continuity or using the isolated intestinal segment representing one form of the urinary bladder substitute. Urine can be directly derivated from the kidney, like in surgical and percutaneous nephrostomy.

Simon is considered to be the first one in the history of urology who performed the urinary derivation by simple ureterostomy in 1875³. Tizzoni and Foggi in 1888 experimentally applied the intestinal segment for the same purpose, while Couvelaire introduced supravesical derivation using the intestine in contemporary surgery^{4,5}. Since then the supravesical urinary derivation has been developed using the most varied methods of the intestinal applications.

Ureteroileocutaneostomy or »the ileum conduit« was introduced by Bricker in 1951 in order to avoid bad points (stenosis and infection) of the direct ureterostomy. The advantages of this method are unquestionable: the possibility of required radical methods in the pelvis and good renal tolerance in this kind of derivation. Bad points are permanent urinary fistula and permanent carrying of the receptacle.

Continent sigma bladder is no doubt the ideal method of preserving physiological and anatomical integrity of the patient7. However, this method is indicated only in primary invasive carcinoma of supratrigonal localisation. The rectal bladder with perineal colostomy according to Nedelec does not leave any physiological orifice the patient would be aware of, enables required radical methods, but it is characterized by greater surgical mortality and greater number of early complications in comparison with other methods⁸. Since late eighties the priority has been given to reservoirs formed by detubularised intestinal segment. The first urinary bladder substitute by detubularised segment of the ileum was published by Giertz in 19579. The technique with 65 cm long and split segment of the ileum has been known as Camey. Hautmann detubulated the segment of the ileum and reconstructed it in the form of the letter W or M^{10} .

Nowadays, the methods of forming isolated urinary continent ileum reservoirs, urinary depots, requesting intermittent catheterization, raise great interest. The first results were presented in 1982 by (Kock)¹¹.

The so called »inner urinary derivations«, like ureterosigmoidostomy, introduced in 1911 by (Coffey) still remained¹². It generates hyperchloremic acidosis. Then ureteroileosigmoidostomy was introduced in order to avoid the aforementioned complications.

Consequently, there are no ideal methods of derivation. Each of them is characterised, except the common

ones, by its specific permanent morbidity, early or late complications, and even a high mortality rate.

Patients and Methods

The goal of this study was monitoring the patients with the urinary bladder cancer in patients over 60 years old who underwent radical surgical treatment at the Department of Urology, University Hospital »Rijeka«, Rijeka, Croatia during the 1972-2008 period. Two thousand four hundred and five patients suffering from this disease were treated and 296 (12.3%) of them underwent radical surgical treatment (Table 1). Most of the patients, 207 (70%) of them, were between 60 and 80 years old. There were 160 (77.4%) male and 47 (22.6%) female patients. Anamnestic haematuria was the most frequent and the most important symptom of the urinary bladder tumour, being constant in 68 (32.9%) patients, frequently intermittent in 48 (23.2%) patients, combined with dysuria in 53 (25.6%) patients or complicated with anuria and uremia in 20 (9.3%) patients. Less frequent symptom was dysuria in 18 (9%) patients.

Diagnostic treatment included IVU, the abdominal or transrectal ultrasonography, cystoscopy, endoscopic biopsy and CT.

The clinical stage of the disease was assessed on the basis of results of the aforementioned procedures and determined using the TNM classification.

The tumours were divided according to the histological criteria on well differentiated (G1), moderately differentiated (G2) and poorly differentiated (G3) (Table 2).

Radical surgical treatment was indicated after the endoscopic verification of the tumour and its TNM and histological classification, depending on the clinical state of the patient. Radical cystectomy, alone or in combination with urethrectomy, was successfully performed in 178 (86%) patients (Table 3). In connection with this operation, the problem of the urinary derivation poses itself. The outer derivation, ureteroileocutaneostomy sec. Bricker was most frequently used in our patients – in 158 (76.3%) of them (Table 4).

We divided our postoperative complications into the early ones and the late ones. There were 74 (35.7%) patients with early postoperative complications (Table 5). Control examinations have been performed in 3-month intervals. The control includes the analysis of laboratory findings and the acidic basal status, abdominal ultrasonography and chest x-ray. The shortest observation lasts three months, and the longest 18 years. The progression of the disease during the observation time implies the occurrence of metastases and the progression of local findings.

Results

During the 1972–2008 period 2,405 patients with the urinary bladder cancer were treated, 296 (12.3%) of whom underwent radical surgical treatment (Table 1)¹³.

TABLE 1
NUMBER OF RADICAL URINARY BLADDER OPERATIONS WITH THEIR ANNUAL DISTRIBUTION

	1972–1980	1981–1989	1990–1999	2000–2008	Total
No. of patients	89	196	637	1483	2405
No. of radical operations	14	23	125	134	296

The progressive increase of newly detected carcinomas and the number of radical operations are evident.

Males have been exposed to a greater than females. The sex ratio is being changed with a change of social role of females. This relation was 8:1 in the early 19th century, being nowadays only 2–3:1 in favour of males. There were 160 males and 47 females in our population over 60 years old.

High frequency of the urinary bladder cancer has been also observed in people who smoke more than 22 cigarettes a day. There were 132 (64%) smokers.

Haematuria is the most frequent and the most important symptom of the urinary bladder cancer. It is either continuous or, frequently, intermittent with intervals without bleeding. It can be macroscopical and microscopical and the level of haemorrhage does not correspond to the tumour volume. Haematuria, alone or combined with dysuria, dominated in our patients - in 188 (91%) of them. The next symptoms were dysuric difficulties characterized by frequent and painful urination in 9% of the patients1. The symptoms caused by distant metastases made the third group. These symptoms were significantly less frequent in this kind of tumour, compared with the other kinds of carcinomas, because about 70% of the carcinomas were localised in the urinary bladder at the moment of the first diagnosis, and only 7% of them showed the clinical signs of distant metastases¹. Most of these tumours are the transitional cell carcinomas. Planocellular tumours make only 5% of the epithelial tumours of the urinary bladder. Finally, 1% of the epithelial tumours belong to adenocarcinomas, which are considered to originate from the aberrant prostatic acinuses. In our population there were 190 (91.6%) patients with transitional cell carcinoma, 12 (6%) patients with planocellular tumours and 5 (2.4%) patients with adenocarcinomas.

The invasive urinary bladder tumour metastasizes in the regional lymph nodes¹⁶. Lymphadenectomy was performed in 148 (71.5%) patients. The nodes were positive in 73 (35%) of them. Haematogenous dissemination regularly develops during the later stage of the disease, involving bones (the pelvis and the lumbar spine), then liver, the kidneys and the lungs.

Discussion

There are three basic characteristics of the urinary bladder tumour, on which the prognosis of the disease and the therapy choice depend: the tendency to wall penetration, the tendency of transitional cell dysplasia and the tendency to change the quality of the mucous membrane of the primary tumour surroundings.

According to TNM classification, T3 stage in 92 (44.4%) patients and T2 stage in 85 (41%) patients were predominant in our study. According to histological criteria the most common stage was G3 stage in 151(73%) patients.

It is very important to make preoperative preparatory measures before bringing decision on surgical treatment. It is especially important for the patients with accompanying diseases that encumber postoperative recovery. There were accompanying diseases in 91 (44%) patients. The most common were: heart and lungs diseases in 49 (23.6%) patients, diabetes in 27 (13%) patients and the diseases of the digestive system in 15 (7.2%) patients.

Radical cystectomy alone or combined with urethrectomy, was performed in 178 (86%) patients (Table 3). Three patients underwent unilateral nephroureterectomy because of renal dysfunction. One uremic patient underwent bilateral nephroureterectomy before the cystectomy was performed. Unfortunately, the inner iliac blood vessels were tied off in 12% of patients (T3 and T4 stages) due to progressive tumours.

The great problem is what kind of urinary derivation has to be done. Demands for normal social activities do not fit into medical criteria, into postulates of radical oncologic surgery especially. Consequently, various non-medical conditions influence the choice of method of derivation: the age of patient, occupation, the stage of civilisation and health education, financial – economic potentials etc. One of the pioneers of modern urology Howard Hanley says that it is a pure hypocrisy from us to claim

Tumour grading	No. of patients (%)
G1	7 (3.4%)
G2	49 (23.6%)
G3	151 (73%)

Type of operation	No. of patients (%)
Radical cystectomy	166 (80.2%)
Radical cystectomy + urethrectomy	12 (5.8%)
Radical cystectomy + nephroureterectomy	4 (1.7%)
Ligatura aa. illiaca	24 (12%)
Cystectomy and resection of colon sygmoideum	1 (0.3%)

that we healed the patient who underwent the abdominal urinary derivation and has been forced to carry the receptaculum under his shirt for the rest of his life¹⁷.

The continent bladder, that would ensure safe excretion under own control and in a standing position (men), most frequently eliminates the possibility of radical intervention (cystourethrectomy). A golden mean that would meet both the criteria has not been found yet. In other words, all kinds of urinary derivations are predominantly methods of necessity.

Modern era of ureterointestinal derivations started in 1911 with Coffey's description of "tunnel" technique for the implantation of ureters into the colon. Ureterosigmoidostomy represented the most popular way of the urinary derivation till 1950, when Bricker described ureteroileal cutaneous derivation. We used this kind of derivation in 10 (4.8%) patients till 1985. This method of supravesical derivation has been almost abandoned nowadays because of numerous complications which can be divided into the early ones and the late ones. The most frequent early complication is anuria developing from the oedema or the obstruction of ureterocolic anastomosis with faeces and the mucous membrane. Urine drainage can occur on the anastomosis with the ileus as the consequence. Late complications are pyelonephritis, calculi, ureteral obstruction and electrolytic instability. Seven of our patients developed hyperchloremic acidosis as the commonest complication. They were treated with bicarbonate compensation. One of them developed paralytic ileus. However, it must not be forgotten that this method has certain advantages, like low immediate operative mortality and morbidity. It is also important to point out that ureterosigmoidostomy does not leave any outer artificial orifice. Making efforts to improve this method because of numerous complications, the ureteroileosigmoidostomy was developed. This is so called antireflux ureterosigmoidostomy or »the inner Bricker«¹⁸. The interposed segment of the ileum, together with antireflux barrier on the anastomosis with the colon, prevents reflux from the large intestine. In spite of the decreased number of manifest pyelonephritises, persistent hyperchloremic acidosis occurred in 1/3 of our patients. This method was performed in 5 (2.4%) of our patients.

Ureteroileocutaneostomy or "the ileum conduit" was introduced by Bricker in order to avoid bad points (stenosis and infection) of the direct ureterostomy. The advantages of this method are unquestionable: the possibility of required radical treatment in the pelvis and good renal tolerance in this kind of derivation. Bad points are permanent urinary fistula and permanent carrying the receptacle. This method of derivation was performed in most of the patients, i.e. in 158 (76.3%) of them (Table 4). It was usually carried out in combination with radical cystectomy or without it in inoperable cases with ligation of the iliac blood vessels. Since late eighties the priority has been given to reservoirs formed by detubulated intestinal segment. Hautmann detubulated the segment of the ileum and reconstructed it in the form of the letter W

TABLE 4
TYPES OF SURGICAL DERIVATION

Type of operation	No. of patients (%)
Ureterosigmoidostomy sec. Coffey	10 (4.8%)
Ureteroileosigmoidostomy	5 (2.4%)
Ureteroileocutaneostomy sec. Bricker	158 (76.3%)
Neovesica sec. Hautmann and Studer	24 (11.5%)
Mainz-Pouch II	2 (1%)
U-nephrostomy and UCNS	5 (2.4%)

or M. Studer (1988) described asymmetrically joined segment of the ileum 65 cm long, in the shorter end which he implanted the ureters. He split longitudinally the longer part and connected it into a hypotonic bladder ^{19–21}. It is especially important because the orthotopic bladder substitute enables the physiological way of urination and higher quality of life. New bladder sec. Hautmann was performed in 23 (11.1%) patients. Neovesica sec. Studer was carried out in one female patient, what is very rare in women. U-tubing nephrostomy or ureterocutaneostomy were performed in the remaining kidney in 5 (2.4%) patients in case of the dysfunction of one kidney or the former nephrectomy. Mainz-Pouch II of the inner derivation was performed in two patients.

There were 74 (35.7%) patients with early postoperative complications. Among them dominated the surgical complications in 28 (13.5%) patients and distant organs complications in 22 (10.6%) patients (Table 5). Wound dehiscence in 9 (4.3%) patients and ileus in 8 (3.8%) patients were the most frequent surgical complications. The secondary sutures were placed in cases of dehiscence. Two patients with the ileus underwent adhesiolysis and one patient adhesiolysis and ileotransversostomy. One ileus was solved with the ileum resection and ileostomy. Four patients with ileus were treated conservatively using Miller-Abbott tube. Bronchopneumonia in 7 (3.4%) patients and cerebral insults in 4 (1.9%) patients dominated among organ complications, and they were treated conservatively. One patient with melena was treated by washing out and blood transfusions. Pyloroplasty and vagotomy were done in one bleeding duodenal ulcer. Two pulmonary embolisms were the most difficult complications which ended lethally. Hyperchloremic acidosis was the most frequent complication in 11 (5.3%) patients connected with operation sec. Coffey and ureteroileosigmoidostomy. It was treated with adequate bicarbonate doses. There were unclear febrile cases among

TABLE 5
EARLY POSTOPERATIVE COMPLICATIONS

Type of complications	No. of patients (%)
Surgical complications	28 (13.5%)
Complications on distant organs	$22\ (10.6\%)$
Metabolic complications	11 (5.3%)
General complications	13 (6.2%)

general complications in 8 (3.8%) patients. Four patients developed septic temperatures. Pseudomonas aeruginosa in 2 patients, Seratia in 1 patient and Staphilococcus pyogenes in 1 patient were isolated in haemoculture. Urinary infection in 12 (5.8%) patients and ileus in 7 (3.4%) patients that were mainly treated conservatively, dominated among late complications. Two patients underwent adhesiolysis. Two ureteral strictures, calculus in the urinary bladder, two ureteral tumours and three ureteral stenoses were treated with endoscopy. There were three stomal stenoses and four stomal hernias that were solved with front abdominal wall plastic. The abscess of postoperative section was treated with the incision and drainage in three patients, while one patient with ureterorrhagia from the residual part of the ureter underwent urethrectomy. One stercoral fistula was solved conservatively. In 75 (36%) patients with negative nodes the survival rate was 55% after five years. In 73 (35%) patients with positive nodes the treatment continued with radiotherapy and chemotherapy. The survival rate was 27% after five years.

The worst prognosis was in the group of patients (12%) in whom cystectomy could not be done due to the progressive process. The iliac blood vessels were tied off in these patients, and they were treated with radiotherapy and chemotherapy. The survival rate was about 7% after one year.

Conclusion

Urinary bladder cancer is the most frequent malignant tumour of the urinary system. It has been in tre-

mendous increase. During 1972-1980 period there were 89 patients and in the 2000-2008 period even 1,483 patients. It is the increase of 27 times, partly because of better diagnostics and education of the inhabitants. Two hundred ninety-six patients underwent radical surgical treatment. Most of them, 207 (70%) patients, were over 60 years old. This population was represented in details. The cancers are more and more malignant and progressive in the diagnostic T3 stage patients (44.4%). Surgical treatment is a method of choice and the way of giving chances for full cure, if carried out in the early stage. The survival rate in this group of patients was 55% after five years. Supravesical urinary derivation is the attractive intervention for the surgeon and desperate solution for the patient, which cannot always fulfil the medical and social aspects of treatment of frequently incurable disease. Medical and social aspects of supravesical urinary derivation most often reciprocally clash, because fulfilling medical criteria aggravates or makes impossible the social life of the patient. The continent bladder, that would ensure safe excretion under own control and in a standing position (in men), most frequently eliminates the possibility of radical treatment (cystourethrectomy). In other words, all kinds of the urinary derivations are predominantly methods of necessity. Thus, majority of our patients (76.3%) have ileostomy, because they underwent surgical intervention in the progressive stage of tumour, and in whom neovesica could not be done due to the progressive process in the pelvis. Finally, the prognosis of the disease and the quality of patient's life depend on as early and as fast as possible diagnosis, as well as on adequate surgical treatment.

REFERENCES

1. LEVIN ML, J Natl Cancer Inst, 24 (1960) 1243. — 2. VEYS C, Br J Ind Med, 31 (1974) 65. — 3. SIMON CJ, Samml Klinik Vort, 88 (1875) 694. — 4. TIZZONI G, FOGGI A, Centrbl Chir, 50 (1888) 921. — 5. COUVELAIRE R, J Urol, 57 (1951) 408. — 6. BRICKER EM, Surgery, 32 (1952) 372. — 7. HRADEC E, Urologie, 2 (1966) 56. — 8. NEDELEC M, Urol Int, 22 (1967) 47. — 9. GIERTZ G, FRANKSSON C, Acta Chir Scan, 113 (1957) 218. — 10. HAUTMANN RE, EGGHARDT G, FROHNEBERG D, MILLER K, Urologie, 26 (1987) 67. — 11. KOCK NG, NILSON AE, NOVLEN L, SUNDIN T, TRASTI H, Scand J Urol Nephrol, 49 (1978) 23. — 12. COFFEY RC, JAMA, 56 (1911) 397. — 13. ĐORĐEVIĆ G, PEITL V, SINOŽIĆ E, MUSTAĆ E, Medicina, 42 (2004) 147. — 14.

FLOCH RH, JAMA, 145 (1951) 295. — 15. NOVAK R, DIMANOVSKI J, FIŠTER H, KRAUS O, TRNSKI D, Lijec Vjesn, 106 (1984) 402. — 16. PUGH RCB, Course of the British Council on urological malignancies, London, 1979. — 17. HANLEY HG, Br J Urol, 39 (1967) 693. — 18. NOVAK R, Eur Urol, 7 (1981) 118. — 19. STUDER U, ACKERMAN D, CASANOVA GA, ZINNG EJ, Semin Urol, 6 (1988) 57. — 20. PETKOVIC M, MUHVIC D, ZAMOLO G, JONJIC N, MUSTAC E, MRAKOVCIC-SUTIC I, SEILI-BEKAFIGO I, Coll Antropol, 28(1) (2004) 337. — 21. VRLJICAK K, MILOSEVIC D, BATINIC D, KNIEWALD H, NIZIC L, Coll Antropol, 30(2) (2006) 355.

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RADIKALNO KIRURŠKO LIJEČENJE KARCINOMA MOKRAĆNOG MJEHURA U BOLESNIKA STARIJIH OD 60 GODINA – NAŠA ISKUSTVA

SAŽETAK

Cilj rada je analiza naših bolesnika starijih od 60 godina oboljelih od raka mokraćnog mjehura, kod kojih je učinjena radikalna operacija mokraćnog mjehura i derivacija urina. U razdoblju od 1972.–2008. liječili smo 2405 bolesnika sa rakom mokraćnog mjehura. Radikalnom kirurškom zahvatu podvrgnuto je 296 (12,3%) bolesnika. Najviše bolesnika je bilo u dobi između 60. i 80. godine (207 bolesnika – 70%). U većine naših bolesnika postavljena je dijagnoza karcinoma prijelaznog epitela (190 bolesnika – 91,6%). Prema TNM klasifikaciji dominira T3 stadij u 92 bolesnika (44,4%) i T2 stadij u 85 bolesnika (41%). Prema histološkom kriteriju najčešći je G3 stadij (151 bolesnik – 73%). Radikalnu cistektomiju samu ili kombiniranu sa uretrektomijom učinili smo kod 178 (86%) bolesnika. U 12% bolesnika (T3b i T4 stadij) podvezali smo samo unutarnje ilijačne žile zbog uznapredovalog tumora. Vanjsku supravezikalnu derivaciju urina (Bricker, U-tubing nefrostomija, ureterokutaneostomija) učinili smo kod 163 (78,7%) bolesnika. Unutarnju derivaciju (Coffey, ureteroileosigmoidostomija, Mainz-Pouch II) rabili smo u 17 (8,2%), a neovesiku (Hautmann, Studer) kod 24 (11,5%) bolesnika. Ranih postoperacijskih komplikacija je bilo 74 (35,7%). Među njima dominiraju kirurške komplikacija u 28 (13,5%) bolesnika i komplikacije udaljenih organa u 22 (10,6%) bolesnika. U 75 bolesnika (36%) sa negativnim čvorovima 5-godišnje preživljenje je bilo 55 %. Kod bolesnika sa pozitivnim čvorovima (73 bolesnika – 35%), 5-godišnje preživljenje je bilo 27%.