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Prostate and Bladder Cancer Coexistence in Patients Undergoing Radical Cystoprostatectomy

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article; **G** – other

Abstract

Background. According to the Polish National Cancer Registry, bladder cancer is the 4th most common cancer in the male population (7.0%), while prostate cancer takes 2nd place (14.0%). In the case of both cancer types, prognoses are precarious and depend on many factors, such as the size of the primary tumor, infiltration of regional lymph nodes, histological grade and occurrence of distant metastases.

Objectives. The objective of this work is to verify the coincidence of prostate cancer and bladder cancer in patients who underwent radical cystoprostatectomy in Wroclaw Medical University, Department of Urology and Oncological Urology, as well as to indicate factors that may influence the peri- and post-operative course.

Material and Methods. We have retrospectively reviewed patients who underwent radical cystoprostatectomy for muscular-invasive bladder cancer between 2009 and 2014, which comprised of 116 male patients. We managed to establish telephone and personal contact with the patients.

Results. Seventeen of the 116 patients were diagnosed with coincidental prostate cancer in post-operative histological examination (14.6%). This result is lower than in other series of cystoprostatectomy cases (range 23–68%). The mean age of patient was 68.9 years and the median was 69.5 years. Factors influencing the peri- and post-operative periods were not statistically significant.

Conclusions. Serum PSA level and DRE should be performed more often on patients prepared for radical cystoprostatectomy. An accurate pre-operative assessment of cancer infiltration is required for both types of tumors. Complete resection of prostate prevents residual neoplasm infiltration. It is important to take into account the possibility of primary prostate tumor occurrence in patients qualified for radical cystectomy. The post-operative supervision should be focused not only on bladder carcinoma but on the prostate carcinoma, too (**Adv Clin Exp Med 2015, 24, 4, 657–662**).

Key words: cystectomy, prostatectomy, bladder cancer, prostate cancer, prostate-specific antigen.

According to the National Cancer Registry, bladder cancer is the 4th most common cancer in the male population (7.0%), while prostate cancer takes 2nd place (14.0%) [1].

In the case of both cancer types, prognoses are precarious and depend on many factors, such as the size of the primary tumor, infiltration of regional lymph nodes, histological grade and occurrence of distant metastases.

While the incidence of bladder cancer continues to decrease in the male population in Poland, the exact opposite trend is being observed as far as the prostate cancer morbidity rate is concerned [2]. Rullis et al., after examinating autopsy material collected from the patients above 80 years of age, stated that prostate cancer prevalence is at 53.0% [3]. More and more precise diagnostic methods as well as the rising social health awareness led to an increase in the detection rate of prostate cancer [4].

Bladder cancer is still often found in the Polish population, in particular at the stage of infiltrating the muscle membrane. Incidence increases significantly in the 7th and 8th decade of life and more frequently (2–3 times) occurs in men [5]. The risk factors for bladder cancer are e.g. smoking, exposure to industrial carcinogens (beta-naphthylamine or

benzidine), lower pelvic radiation and *Schistosoma haematobium* infection. The latter is the most frequent cause of cancer in developing countries, since it predisposes to squamous cell carcinoma. Some drugs (cyclophosphamide) also make patients more likely to develop bladder cancer. Intercurrence of both types of cancer in one patient was described in the world literature. Supposition of an increased risk of bladder and prostate cancer comorbidity was put forward already in the 1950s [6].

The region of residence of the observed population and the consequent diversification of risk factors may exert impact on the coincidence of both tumors. The percentage of coexisting cancer types varies from a few % [7] up to 45.0% [9]. According to the result of the research carried out by Pritchett et al. in the U.S. population, the percentage of coincidences stands at 27% [10], while in the Japanese population Yumura et al. diagnosed primary prostate cancer in 17 out of 299 (5.9%) patients treated initially for bladder cancer [11]. Sanli et al. performed radical cystoprostatectomy in the group of 97 patients suffering from bladder cancer. Simultaneous coexistence of prostate cancer was found in 21 (21.6%) of these cases [12]. During the research carried out by Abdelhadey et al. prostate cancer was detected in 58 (26.7%) patients out of the group of 217 men who underwent radical cystoprostatectomy; the Gleason Score equal to or greater than 7 was observed in 12 out of 58 men (20%) [13]. Referring to Chun et al. the risk of developing prostate or bladder cancer in patients with another diagnosed type of cancer increases 18 times [14].

Material and Methods

One hundred sixteen male patients undergoing radical cystoprostatectomy due to invasive bladder cancer were retrospectively analyzed in the Department of Urology and Urological Oncology, Wroclaw Medical University over the period 2009–2014.

In 17 out of 116 patients (14.6%) the primary prostate cancer was found during the postoperative histologic examination. In 16 out of 17 (94.1%) cases the diagnosis of prostate cancer was incidental, thus the remaining one was detected before surgery in the DRE (Digital Rectal Examination) and confirmed by prostate transrectal biopsy.

Ninety nine remaining patients were diagnosed with bladder cancer only.

The average age of patients who underwent radical cystoprostatectomy is 68.9 years (range from 56 to 81 years), as the median was 69.5 years. 10 out of 17 patients (58.8%) were interviewed. As far as 5 patients are concerned, the attempt to establish the contact failed, while the remaining 2 patients were found dead. In the postoperative period none of the patients were treated with an 5-alpha-reductase inhibitor (finasteride).

Results

In the case of both neoplasm/cancer types, the disease stage was assessed according to TNM 2010 classification – based on the postoperative histological examination results. The incidence of cancer diagnosed in different stages was as follows (the T feature):

Bladder cancer was diagnosed as follows (presented in Fig. 1):

Tis – 2 patients
T1 – 1 patient
T2 – 2 patients
T3 – 3 patients
T4 – 7 patients

Regional lymph nodes were positive in 5 patients (carcinoma urotheliale).

Prostate cancer was diagnosed as follows (presented in Fig. 2):

T1 – 3 patients
T2 – 9 patients
T3 – 5 patients

T4 stage did not occur in any of the patients.

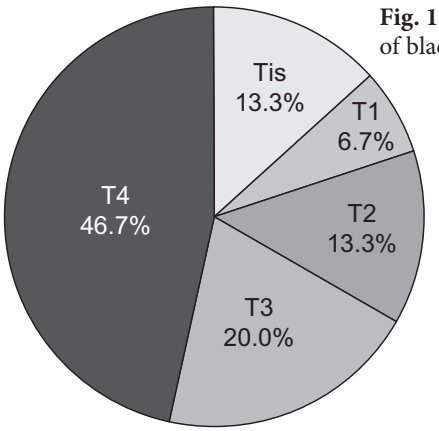

Fig. 1. T feature of bladder cancer

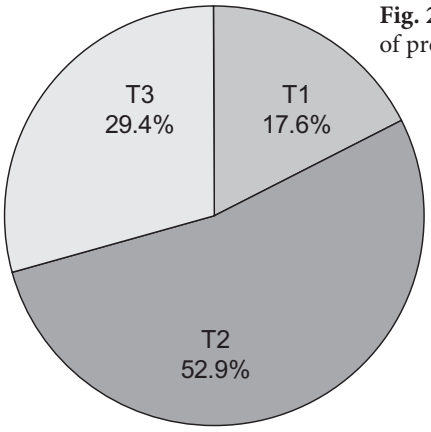

Fig. 2. T feature of prostate cancer

Table 1. Gleason Score and TNM staging according to each patient

Patient	Gleason Score	TNM 2010 staging
1	3 + 3 = 6	pT2aN0
2	3 + 3 = 6	pT2cN0
3	3 + 3 = 6	pT2aN0
4	4 + 5 = 9A	pT3bN0
5	3 + 3 = 6	pT2cN0
6	3 + 3 = 6	pT3bN0
7	2 + 3 = 5A	pT1N0
8	3 + 2 = 5B	pT1aN0
9	4 + 5 = 9A	pT3bN1
10	5 + 5 = 10	pT2cN0
11	3 + 4 = 7A	pT2cN0
12	5 + 4 = 9B	pT3aN0
13	5 + 5 = 10	pT3bN0
14	3 + 3 = 6	pT2aN0
15	5 + 4 = 9B	pT2cN0
16	3 + 3 = 6	pT1bN0
17	3 + 3 = 6	pT2cN0

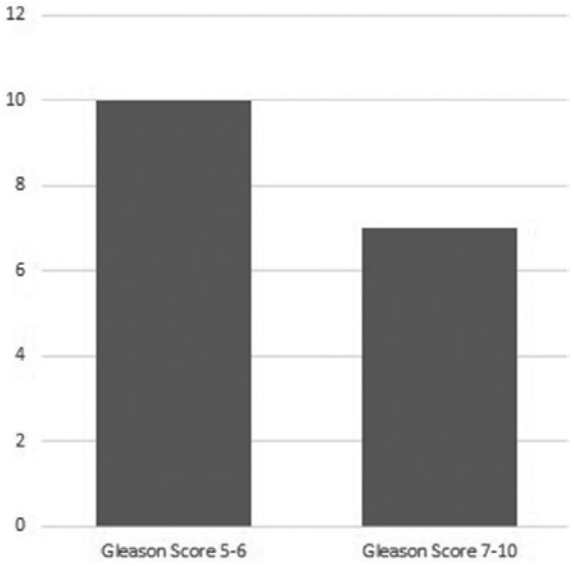

Fig. 3. Gleason Score results divided in groups (up to 6 and 7 or greater)

Regional lymph nodes were positive in 1 patient (adenocarcinoma).

In 7 out of 17 patients (41.2%) with diagnosed prostate cancer, the Gleason Score was greater than or equal to 7. The most common result was Gleason Score 3 + 3 = 6, observed in 8 out of 17 patients (47.1%), which is presented in Table 1 and Fig. 3.

As Table 2 shows, in 6 out of 17 patients (35.3%) cancer infiltrated one lobe of the prostate, with no infiltration of the capsule and seminal vesicles. In another 6 patients (35.3%) cancer infiltrated both lobes of the prostate, without infiltration of the capsule and seminal vesicles. In 4 out of 17 patients (23.5%) cancer infiltrated both lobes of the prostate with the capsula and seminal vesicles. Only in 1 patient (5.8%) cancer infiltrated both lobes of the prostate with the capsule but without infiltration of the seminal vesicles.

Table 2. Local tumor invasion in each patient

Patient	1-infiltration of one lobe 2-infiltration of two lobes	Infiltration of seminal vesicles	Infiltration of prostate's capsula
1	1	0	0
2	2	0	0
3	1	0	0
4	2	1	1
5	2	0	0
6	1	0	0
7	1	0	0
8	2	0	0
9	2	1	1
10	2	0	0
11	2	0	0
12	2	0	1
13	2	1	1
14	1	0	0
15	2	0	0
16	1	0	0
17	2	1	1

The serum PSA (Prostate Specific Antigen) level was determined prior to surgery in 7 patients (41.2%) and the examination revealed an abnormal PSA level in 2 patients, e.g. high for their age. In 5 remaining patients the PSA level was measured postoperatively, in 2 cases the serum PSA level exceeded standard limit values. In 5 out of 17 patients (29.4%) the serum PSA level was tested neither before nor after the surgery. An abnormal PSA level was detected in 4 out of 12 patients. The data on complete blood count, INR, APTT, serum of creatinine, sodium and potassium, collected from 17 patients with 2 primary cancers was compared with the corresponding data collected from 99 patients with solitary bladder cancer (Table 4).

By comparing these 3 groups, the following parameters were taken into consideration: complete blood count, INR, APTT, serum of creatinine, sodium, potassium (Table 4).

Comparing these groups the parameters such as GFR, BMI, time to realimentation after surgery, time to drainage removal, time of hospitalization after operation, length of operation and intraoperational blood loss (Table 5) does not show any significant differences.

As Table 6 shows, the Charlson Comorbidity Index was determined for each patient.

Table 3. Time of PSA level determination (before or after cystectomy) and its value in relation to existence of neoplasia

Patient	Serum PSA level (ng/mL)	0 – PSA level correct 1 – PSA level above the norm x – PSA level not examined	0 – PSA examined before operation 1 – PSA examined after operation	0 – prostate cancer not diagnosed before operation 1 – prostate cancer diagnosed before operation
1	0.01	0	1	0
2	0.93	0	0	0
3	x	x	x	0
4	8.68	1	0	0
5	0.06	0	1	0
6	x	x	x	0
7	x	x	x	0
8	2.81	0	0	0
9	10.45	1	0	1
10	12.34	1	1	1
11	0.92	0	0	0
12	x	x	x	0
13	5.87	1	1	0
14	x	x	x	0
15	2.41	0	0	0
16	1.97	0	0	0
17	0.04	0	1	0

Table 4. Average blood tests parameters in each group of patients

Parameter (average/ /median)	Patients with both coexisting neoplasms	Patients with isolated bladder neoplasm
WBC	9.08/8.80	9.63/8.61
RBC	4.24/4.20	4.35/4.34
Hb	12.47/12.20	12.96/12.80
MCV	89.24/89.70	88.61/88.65
MCH	29.34/29.30	29.24/29.20
MCHC	33.39/33.00	32.96/33.00
PLT	263/250	293/272
MPV	10.59/10.40	10.28/10.20
INR	1.01/1.00	1.00/0.99
APTT	31.60/30.30	29.79/29.16
Creatinine	1.38/1.27	1.32/1.28
Sodium	139/140	138/139
Potassium	4.29/4.20	4.40/4.39

Table 5. Average GFR level, BMI and hospitalization parameters in both groups of patients

Parameter (average/median)	Patients with coexisting both types of neoplasms	Patients with isolated bladder cancer
GFR	61.93/58.65	71.02/66.81
BMI	26.70/25.14	27.00/26.42
Time to realimentation	4.80/5.00	4.93/5.00
Time to drainage removal	6.06/6.00	6.45/5.00
Time of hospitalization after operation	12.53/12.00	15.56/14.00
Length of operation	4.71/4.50	5.20/5.00
Intraoperational blood loss	1105/1000	943/825

Patients undergoing radical cystoprostatectomy are burdened with numerous comorbidities, such as arterial hypertension, diabetes mellitus and so forth (Table 7).

Ureterohydronephrosis before treatment was observed in 5 out of 17 patients. Urinary diversion has been performed as follows: 11 patients (64.7%) Bricker method, 3 patients (17.6%) ureterocutaneostomy and in 2 patients (11.8%) orthotopic ileal neobladder. Red blood cells transfusion was performed in 7 patients (41.2%), while the average number of units given was 1.69. In a 30-day postoperative period 2 patients died.

Post-surgical complications occurred in 10 out of 17 patients. The most frequent complication was high fever – the indication of infection, which occurred in 9 patients (52.9%). The next most frequent were cardiological complications – acute myocardial infarction – which occurred in 2 patients (11.8%).

In 6 patients (35.3%) the coincidence of primary prostate cancer with infiltration of bladder

Table 6. Risk of death based upon coexisting diseases (Charlson Comorbidity Index)

Charlson Comorbidity Index	Patients with coexisting both types of neoplasms	Patients with isolated bladder neoplasm
1	0 (0.0%)	0 (0.0%)
2	0 (0.0%)	4 (4.0%)
3	0 (0.0%)	14 (14.1%)
4	1 (5.8%)	17 (17.2%)
5	0 (0.0%)	12 (12.1%)
6	6 (35.3%)	16 (16.2%)
7	3 (17.6%)	12 (12.1%)
8	4 (23.5%)	10 (10.1%)
9	2 (11.8%)	5 (5.1%)
10	0 (0.0%)	6 (6.1%)
11	0 (0.0%)	1 (1.0%)
12	0 (0.0%)	0 (0.0%)
13	0 (0.0%)	1 (1.0%)

cancer to prostate was observed. In 4 of them (66.7%) the Gleason Score was higher than or equal to 7 points.

As Table 8 shows in the group of 17 patients with coexisting both types of neoplasms, 2 deaths in postoperative period (up to 30th day after surgery) occurred. However, it is important that this treatment had a palliative character and the T stage was estimated as T4. Clavien-Dindo grading system was used for the classification of surgical complications.

Within a one-month period from the surgery 2 patients died and 4 patients died within 12 months from the surgery. Twelve-month survival rate is 58% (7 out of 12 followed-up patients survived 12 or more months), whereas no contact was established as far as 5 remaining patients are concerned.

In the 5-year reference period 4 patients (out of 116 patients observed) died (3.5%).

Discussion

Within the research group of 116 patients 12 patients (70.6%) were diagnosed with prostate cancer at stages T1–T2. In 10 patients (58.8%) the Gleason Score was estimated at the level of 5–6 points. As far as the PSA is concerned, the test was performed in 12 patients (70.6%) but only in 7 patients (41.2%) pre-operatively, while 5 patients (29.4%) were not examined for PSA level at all. Just 2 patients (11.8%) underwent the pre-operative prostate biopsy, one of which was negative, i.e. the carcinomatous tissue was not found, whereas the other patient was diagnosed with prostate cancer pre-operatively.

In the diagnosis of prostate cancer the ultrasound-controlled transrectal prostate biopsy with 12 specimens (6 for each lobe) for histopathological examination is the golden standard. However, performing both digital rectum examination (DRE) and PSA test is the very least in oncological diagnosis of prostate. Screening procedures aimed at identifying prostate cancer were not adopted in Poland yet; however, experts recommend performing DRE and serum PSA tests in men above 45 years old within each visit at the general practitioner. If the level of serum PSA, which is considered to be the most organ-specific neoplasmatic antigen, is elevated, the blood test should be followed by DRE or even prostate biopsy, if necessary.

The abovementioned research results indicate that patients with diagnosed muscle-invasive bladder cancer should be tested for the PSA level and undergo the DRE more frequently. Furthermore, in patients with an incorrect serum PSA level or oncologically alerting DRE the USG-controlled transrectal prostate biopsy should be performed.

Early on, the prostate cancer is usually asymptomatic or oligosymptomatic, hence performing

Table 7. Pre-operative diseases

Pre-operative diseases	Arterial hypertension	Positive heart infarct anamnesis	Diabetes melitus	Status post abdominal operation
Patients with coexisting both types of neoplasms	8 (47%)	3 (17.6%)	2 (11.8%)	2 (11.8%)
Patients with isolated bladder neoplasm	50 (50.5%)	27 (27.3%)	16 (16.2%)	17 (17.2%)

Table 8. Post-operative complications (estimated by Clavien-Dindo scale)

Clavien – Dindo	I	II	III	IV	V
Patients with coexisting both types of neoplasms	5 (27.4%)	9 (52.9%)	0 (0.0%)	1 (5.9%)	2 (11.8%)
Patients with isolated bladder neoplasm	27 (27.3%)	54 (54.5%)	7 (7.1%)	8 (8.1%)	2 (2.0%)

serum PSA tests as well as DRE by general practitioner – as a normal practice – is desirable. With a reference to the research results, one draws the conclusion that the coincidence of prostate cancer in patients undergoing cystoprostatectomy for muscle-invasive bladder cancer influences neither the surgery itself nor the post-operative period. Statistically significant differences were not found.

The post-operative mortality rate positively correlates with bladder cancer clinical staging and with coexisting diseases but does not correlate with prostate cancer stage.

Another conclusion arrived at by analysing the collected data is the necessity of pre-operative, very accurate estimation of cancer infiltration not only in the bladder, but also in the prostate. The resection of the prostate should be complete – it prevents residual neoplasm infiltration and the necessity of post-operative radiation therapy.

Within the diagnostics of bladder cancer, it is important not to forget about the possibility of coexistence of primary prostate cancer. In the case of coincidence of both cancer types, the post-operative supervision (after radical cystoprostatectomy for muscle-invasive bladder cancer) should include an observation of eventual progression of prostate cancer.

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