

COMPARISON OF PREOPERATIVE AND POSTOPERATIVE STAGE AND GRADE OF PROSTATE CARCINOMA IN PATIENTS WITH PSA LEVEL OF 2-10 NG/ML

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Summary

Patients are selected for radical prostatectomy with a disease limited to the organ, satisfying general condition and enough long life expectancy. Postsurgical findings often point out more advanced disease or less differentiated cancer compared to findings upon which an indication for prostatectomy was made, what affects prognosis and points out need for adjuvant treatment.

The study is aimed at establishing in what manner the clinical stage and grade of the disease correlate to the definitive histological finding.

The investigation was done in 80 patients with histologically proven, clinically organ confirmed prostate cancer, and initial PSA values 2-10 ng/ml, which underwent retro-pubic prostatectomy. Pathohistological analysis of complete resection sample was performed in order to establish spread and differentiation of the tumor. Clinical and pathological stage of the disease, Gleason score and Gleason grade were compared.

In 11 patients (14%) extra-prostatic invasion of the disease was found following examination of the obtained slides. After surgery, in a significant number of patients inclusion of both prostate lobes was established, so the number of clinical stage T2b was significantly higher than pT2b (40 compared to 18), and T2c was significantly lower than pT2c (3 compared to 22). The Gleason score was underestimated in 25 (31, 25%) while it was overrated in 2 (2.5%).

In more than one-third of patients the bioptical Gleason score was lower than the definitive pathohistologic score of the prostate slide. There is a significant difference between the biopsy and definitive pathohistologic T stage of prostate cancer also in a sense of underestimation. The frequency of established extra-capsular invasion and lymphatic metastasis corresponds to the rates of predictive models (Partin tables). The study did not show extra-capsular invasion in cases of well-differentiated prostate cancer (Gleason score ≤ 6).

KEYWORDS: *prostate cancer, tumor stage, tumor grade*

USPOREDBA PREOPERATIVNOG I POSTOPERATIVNOG KLINIČKOG STADIJA I GRADUSA KARCINOMA PROSTATE U BOLESNIKA S VRIJEDNOSTIMA PSA 2-10 NG/ML

Sažetak

Za radikalna prostatektomiju selekcioniraju se pacijenti s na organ ograničenom bolešću, zadovoljavajućem općem stanju i dovoljno dugim očekivanim preživljenjem. Postoperativni nalazi često upućuju na veću uznapredovalost ili slabiju diferenciranost karcinoma u odnosu na nalaze na osnovi kojih je postavljena indikacija za kirurški zahvat, što utječe na prognozu i upućuje na potrebu adjuvantnog liječenja.

Cilj rada je utvrditi u kojoj mjeri klinički stadij i gradus bolesti odgovaraju definitivnim patohistološkim nalazima kod pacijenata kod kojih je preoperativno postavljena dijagnoza na organ ograničenog karcinoma prostate i učinjena radikalna prostatektomija.

Ispitivanje je provedeno kod 80 pacijenata s histološki dokazanim karcinomom prostate, vrijednostima PSA od 2 do 10 ng/ml, klinički na organ ograničenom bolešću, te učinjenom retropubičnom radikalnom prostatektomijom. Napravljena je

patohistološka analiza kompletnog reseciranog materijala sa ciljem utvrđivanja uznapređivosti i diferenciranosti tumora. Uspoređivan je klinički i patohistološki stadij bolesti, te Gleason skor i Gleason gradus karcinoma postavljen na osnovi pregleda biopsijskog materijala s istim pokazateljima diferenciranosti tumora utvrđenim u materijalu dobivenom radikalnom prostatektomijom.

Pregledom definitivnog preparata kod 11 pacijenata (14%) utvrđena je ekstraprostatična ekstenzija bolesti. Kod značajnog broja postoperativno je utvrđena zahvaćenost oba lobusa prostate, tako da je u definitivnom preparatu prostate broj kliničkih u odnosu na patološki stadij T2b znatno manji (40 u odnosu na 18), a T2c znatno veći (3 u odnosu na 22). Biopsijski Gleason skor podcijenjen je u odnosu na Gleason skor preparata prostate kod 25 (31.25%), dok je precijenjen kod 2 (2.5%). Kod više od trećine pacijenata u biopsijskom preparatu Gleason skor niži je u odnosu na definitivni patohistološki Gleason skor preparata prostate. Postoji značajna razlika između biopsijskog i definitivnog patohistološkog T stadija karcinoma prostate također u smislu podcjenjivanja. Učestalost utvrđenog ekstrakapsularnog širenja i limfnih metastaza odgovara stopama prediktivnih modela (Partinove tablice). U provedenom istraživanju ekstrakapsularno širenje nije nađeno kod dobro diferenciranih karcinoma prostate (Gleason skor ≤ 6).

KLJUČNE RIJEČI: *karcinom prostate, stadij tumora, gradus tumora*

INTRODUCION

Anatomic progression (stage of the disease), level of differentiation, (tumor grade) and level of serum prostate specific antigen (PSA) (1, 2) are basic parameters on which therapeutic decision and prognosis of the disease is based in prostate cancer. Clinical stage, mostly defined by the TNM classification, is established by digital rectal examination, and depending on its findings, symptoms and other parameters on trans-rectal ultrasound, CT scan, MRI, bone scintigraphy (3, 4). The most important purpose of the procedure is to differentiate organ-limited, locally advanced and disseminated disease, which is approached by therapy in a different manner.

Tumor differentiation correlates with malignant potential of the disease and influences significantly its prognosis (5). The Gleason classification is the most commonly accepted today, and it uses the numeric scale from 1 to 5 for characterization of histological finding of two or more cancer specimens and their score - Gleason score (GS) (6, 7). Well-differentiated tumors - G1 have GS 2-4, medium differentiated (G2) GS 5-7, and weakly differentiated (G3) GS 8-10.

Exact data on the size and progression of the tumor and its differentiation are obtained from histological sampling of tissue resected during radical prostatectomy, and in that manner are definitive, pathohistologic stage and grade of prostate cancer determined (8, 9). However, the disproportion is evident between clinical and pathological stage and disease grade. The underestimation is common and overestimation is less often, which

is reflected in the selection of the next stage of treatment and its final result.

The aim of the study is to analyze the proportion of correspondence between clinical and pathological stage and grade of the disease in patients undergoing radical prostatectomy.

CLINICAL SAMPLE AND METHODS

The study was done in patients with histologically proven prostate cancer, initial PSA values 2-10 ng/ml, palpatory, ultrasound and radiologically verified tumor limited to the organ, and who underwent radical retro-pubic prostatectomy. According to the present guidelines, these patients are considered to be surgically treatable with low likelihood of the existence of locally advanced or disseminated disease. Pathohistologic analysis of the complete material obtained from radical prostatectomy was done in order to establish the size, localization, spread and differentiation of the tumor. Preoperatively established anatomic progression of the disease (clinical stage), Gleason score and Gleason grade were compared with pathohistologic stage and grade determined by histological analysis of the complete resection material.

RESULTS

The study included 80 patients, age range 52-70 years. The average age of the participants was 66 years.

The most common preoperative stage of the disease was T2a, found in 40 patients (50%). The

Table 1.

BASIC PREOPERATIVE PARAMETERS OF PROSTATE CANCER

Parameters	Arithmetic mean	Standard deviation	Range	Variance
T stage ¹	2.21	0.75	1-4	0.57
Gleason score	5.95	1.15	3-7	1.33
G grade	2.51	0.81	1-3	0.65

¹ T stage is in database noted for stage T1c with number 1, T2a number 2, T2b number 3 and T2c number

most common Gleason score (GS) in biopsy samples was 6, found in 31 patients (38%), and G2 grade in 65 (81%) patients. Table 1 shows the range of values of investigated parameters, arithmetic mean, standard deviation and variance of observed variance.

Frequency of single clinical and pathological stages is shown in Table 2. The most significant difference is observed in clinical and definitive stage T2a (40 versus 18), and T2c (3 versus 22). T-test based on the difference of arithmetic mean

Table 2.

CLINICAL AND PATHOHISTOLOGICAL T STAGE OF PROSTATE CANCER

Clinical T stage	N°	Percentage	Pathohistological T stage	N°	Percentage
T1c	13	16%	pT1c	0	0%
T2a	40	50%	pT2a	18	23%
T2b	24	30%	pT2b	32	40%
T2c	3	4%	pT2c	22	27%
T3a	0	0%	pT3a	7	10%
T3b	0	0%	T3b	0	0%
T4	0	0%	T4	0	0%
TOTAL	80	100%	TOTAL	80	100%

Table 3.

BIOPTICAL GLEASON SCORE AND GLEASON SCORE OF DEFINITIVE PROSTATE SPECIMEN

Bioptical GS	N°	Percentage	Definitive GS	N°	Percentage
Gleason score: 2	0	0%	Gleason score: 2	0	0%
Gleason score: 3	2	3%	Gleason score: 3	1	1%
Gleason score: 4	9	11%	Gleason score: 4	6	8%
Gleason score: 5	16	20%	Gleason score: 5	13	16%
Gleason score: 6	31	38%	Gleason score 6	23	29%
Gleason score: 7	22	27%	Gleason score: 7	34	42%
Gleason score: 8	0	0%	Gleason score: 8	3	4%
Gleason score: 9	0	0%	Gleason score: 9	0	0%
Gleason score: 10	0	0%	Gleason score: 10	0	0%
TOTAL	80	100%	TOTAL	80	100%

(1.28) and the difference of standard deviation 0.97, with freedom degree DF=79, strength t=11.86 and 95% safety showed a statistically significant difference between clinical and pathological T stage at the level of significance p<0.05.

The bioptical GS and GS from the definitive finding are shown in Table 3. The most significant differences are found in GS 6 (31/23) and GS 7 (22/34). The significant difference in frequency is also seen in GS 3+4 and 4+3 (14 versus 15 and 18 compared to 19). The bioptical Gleason score is

understaged compared to the prostate specimen Gleason score in 25 (31.25%), while it is overstaged in 2 (2.5%). Insight into t-test between the bioptical and definitive GS shows a statistically significant difference at the level of significance p<0.05, and with arithmetic mean of 0.37 and standard deviation 0.97, and freedom degree DF=79, this t-test demonstrates t=3.44 with 95% certainty.

Table 4 shows the grade of cell differentiation (G stage) in the bioptical and definitive specimen. Arithmetic mean differences were established to

Table 4.

CLINICAL AND PATHOHISTOLOGICAL G STAGE OF PROSTATE CANCER

Bioptical G stage	N°	Percentage	Pathohistological G stage	N°	Percentage
G1	13	16%	G1	7	9%
G2	65	81%	G2	67	84%
G3	2	3%	G3	6	8%
TOTAL	80	100%	TOTAL	80	100%

Table 5.

CLINICAL- PATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH EXTRA-CAPSULAR INVASION

Parameters	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Bioptical Gleason score	7(3+4)	7 (4+3)	7 (4+3)	7(3+4)	7(3+4)	7 (4+3)	7 (4+3)
Clinical stage of tumor	T2c	T2b	T2b	T2b	T2a	T1c	T2b
Bioptical tumor grade	G2	G2	G2	G2	G1	G2	G2

Table 6.

CLINICAL-PATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH LYMPHATIC METASTASIS

Parameters	Patient 1	Patient 2	Patient 3	Patient 4
Bioptical Gleason score	7 (4+3)	7 (4+3)	7 (4+3)	7 (4+3)
Clinical stage of tumor	T2b	T2c	T2b	T2b
Histological stage of tumor	G2	G2	G2	G2

be on the borderline of statistical significance ($p=0.05$, with coefficient of difference of 0.11 and coefficient of differences of standard deviation 0.50, with degree of freedom $DF=79$, t-test 2.00 with 95% safety).

In investigated sample of 80 patients with clinically estimated prostate cancer limited to organ and PSA values of 2-10 ng/ml, in which was performed radical prostatectomy, extra capsular invasion was found in 7, and lymph nodes inclusion in 4. Characteristics of patients with listed pathohistological stage of the disease are presented in Tables 5 and 6.

DISSCUSSION

Patients with disease limited to organ, satisfying general condition and expected long enough survival are selected for radical prostatectomy (2). Postoperative findings often point out to more advanced or worse differentiation of the cancer com-

pared to findings which lead to the indication for surgery what affects prognosis and points out need of adjuvant treatment (9).

The study included a total of 80 patients with according to all criteria operable and most likely treatable prostate cancer: age under 70 years, PSA values 2-10 ng/ml, histologically proven cancer without clinical signs of extra-prostatic invasion. Radical retro-pubic prostatectomy was performed in all patients.

Based on frequencies and percentage of clinical and definitive histological T stage we may note that there is a significant difference. Postoperative histological analysis of the sample demonstrates higher tumor invasion versus preoperative findings. Stage T2c was found preoperatively in only 3 patients, and pT2c in 22 patients. Before the surgery the tumor limited to less than 50% of one prostate lobe (stage T2a) is found in 40, and after surgery in only 18 patients. The number of understaged disease cases is significant in all studies and is reported in 30-40% of patients (9-11). According to the Partin tables, extra-capsular invasion of prostate cancer with PSA values of 2-10 ng/ml dependent on clinical stage and GS varies from 1 to 6% (12, 13). In this study, extra-capsular invasion of the tumor was verified histologically in 7 (9%) patients out of whom 4 had clinical stage T2b and others clinical stages T1c, T2a and T2c, respectively.

According to the Partin tables, lymphatic metastasis prediction was 1-13% (12). In this study, 4 (5%) patients had metastasis to lymph nodes.

Based on this investigation, the bioptical Gleason score compared to the Gleason score of prostate specimen was understaged in 25 (31.25%), while it was overstaged in 2 (2.5%) patients. According to the literature, this concordance in tumor grade is 23-60% (14). The Gleason score in biopsies and radical prostatectomy specimen points out to discordance of results in 40% to 67% of patients (15,16). The pathohistological finding of bioptical sample most often understages the real differentiation of the tumor.

Based on the above listed results we may conclude that:

- In more than one-third of patients the Gleason score in bioptical specimen is lower compared to the definitive pathohistologic Gleason score of the prostate (understaging).
- There is a significant difference between bioptical and definitive pathohistologic finding in prostate cancer also in a sense of clinical understaging of the disease spread.
- Frequency of extra-capsular invasion and lymphatic metastasis responds to the rates of accepted predictive models (Partin tables).
- In this study, histologically proven extra-capsular invasion is not found in well-differentiated prostate cancer (Gleason score \leq 6).

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