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Prognostic Values of Morphological and Clinical Parameters in pT2 – pT3 Prostate Cancer in Elderly People

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A B S T R A C T

Prostate cancer is a disease of elderly men, hthe incidence of whic increases in an age dependent manner. This study presents the correlation of clinical and morphological parameters in locally confined (pT2) and locally advanced (pT3) prostate cancer. We analyzed a group of elderly men treated with radical prostatectomy in the period 1999–2008 in the University Hospital Rijeka. We found no statistical association between pT stage and age categories, preoperative prostate-specific antigen, digitorectal examination and biopsy Gleason score. There was a significant correlation of higher Gleason score in prostate specimens after radical prostatectomy and a higher frequency of a positive surgical margin in tumors with pT3 than in pT2 stage (p=0.003; p=0.011 respectively). Recurrence-free survival was shorter in patients with tumors with positive surgical margins as well as in patients with pT3 stage (p=0.030; p=0.001 respectively). We conclude that higher tumor grade and positive surgical margins are indicators of a worse prognosis in our patients.

Key words: *prostatic neoplasms, prostatectomy, prostate-specific antigen*

Introduction

Prostatic carcinoma is known to be primarily a disease of elderly men, the incidence of which increases in an age dependent manner**.** The incidence of prostate cancer varies throughout the world but it is generally higher in developed western countries with trend of 900,000 newly diagnosed cases per year till 2010[1–3]. The incidence has been increasing due to a multitude of factors such as a wide use of serum prostate-specific antigen (PSA) assay, the introduction of systematic 12-cylinder ultrasound-guided prostate biopsy, an ageing population with longer life expectancy and a general increase in awareness among doctors. As a result of widespread testing of patients for PSA most patients present with clinically localized tumors and low Gleason scores (<6)[4,5]. The natural course of this disease is long and extremely variable with the potential for progression, often during more than 10 years[4,6]. Many clinicians have long believed that prostatic carcinoma takes a less aggressive course in older patients and suggest that no active therapy is necessary for patients with tumors confined to the organ[5,7]. However, in discussing treatment options, watchful waiting is rarely chosen by patients because of fear of future consequences[8]. Recent studies favours early, agressive treatment which provides not only a chance to eradicate prostate cancer, but offers to otherwise healthy older men with reasonable life expectancy, prevention of metastasis and recurrence of the cancer. Potentially curative therapy results in significantly improved life expectancy and quality of life for older men with few comorbidities and moderately or even poorly differentiated localized prostate cancer. Therefore, elderly should not be denied this way of treatment on the grounds of age alone[6,8–10].

The aim of the present study was to establish the differences and associations of clinical and morphological

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parameters with locally confined (pT2) and locally advanced (pT3) prostate cancer in a group of elderly men treated with radical prostatectomy.

Patients and Methods

The study included medical records of patents from the Department of Urology and Department of Oncology and Radiotherapy Rijeka University Hospital Center in Rijeka and files kept at the Department of Pathology, Rijeka University School of Medicine, Rijeka, Croatia.

In the period from 1999 to 2008, 1758 patients were submitted to ultrasound guided needle biopsy and got diagnosis of prostatic adenocarcinoma. Candidates for radical prostatectomy according to the European Association of Urologya criteria had Gleason score 7 or less, PSA less than 10 ng/mL and clinical stage of organ confined prostate cancer T1c/T2c (preoperatively normal findings of pelvic computed tomography and bone scintigraphy)[11]. We separated the group of elderly patients according to the conventional definition, »elderly« has been defined as a chronological age of 65 years old or older[12]. Conventionally, »elderly« has been defined as a chronological age of 65 years or older, while those from 65 to 74 are referred to as »early elderly« and those over 75 as »late elderly«[12]. We divided early elderly in 2 groups: before and after 70. Inclusion criteria were fulfiled in 97 patients, 76 patients of them had postoperative pathological stage (pT2) and 21 had pT3. Clinical and pathomorphological prognostic parameters that we considered were: age, PSA value at the time of diagnosis, digitorectal examination (DRE), Gleason biopsy score, Gleason score in surgical specimen and positive or negative surgical margins. Median follow-up time of patients was 44 months (range 7–129 months) and included oncological and urological control. Clinical and morphological characteristics between the stages were studied and correlated.

A statistical analysis was performed using Statistica 6.1 software (StatSoft, Inc., Tulsa, OK, USA). Mann-Whitney U-test was used to assess the significance of association of pT2 and pT3 stage with clinicopathologic data such as age, PSA, Gleason score of biopsy and Gleason score of a surgical specimen. The association between DRE, patients age and surgical margin with pT2 and pT3 stage was evaluated using χ^2 test. Recurrence-free survival analysis was carried out with the Kaplan-Meier method. Statistical differences with p value less than 0.05 were considered significant.

Results

We found no statistical association between age categories and pT stage (Figure 1).

The evaluation of the number of prostatectomy and prostate cancer diagnosies in Rijeka University Hospital Center is showing a rapid increase of the rate of prostate cancer diagnosies after the year 2001 (Figure 2). The number of prostate cancer diagnosies was 87 in 2001 and 295 in 2008. Also, the number of prostatectomy increased. The most of them were retropubic. We introduced recently a laparoscopic technique in daily practise.

The pathological stage of patients with prostate cancer was compared to clinical parameters such as patients' age, total serum PSA concentration and DRE (Table 1). A statistical analysis showed no significant association of age, PSA concentration and DRE to pT of the disease. Total serum PSA concentrations between pT groups demonstrated higher values in patients presented with pT2 stage (7.5 ng/mL) than in those with pT3 (6.4 ng/mL), but with higher maximal values in these patients (range 5–37.4). Pathological stage of patients with prostate cancer was also compared to pathomorphological parameters as Gleason score before and after the

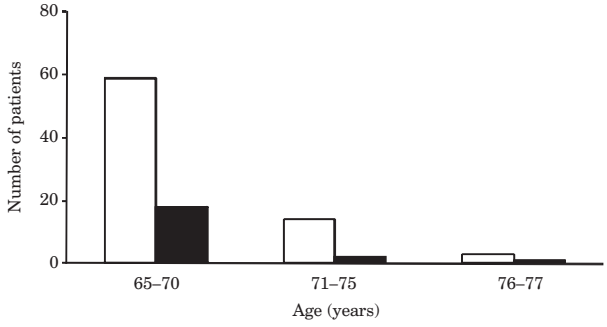

Fig. 1. Pathological stage (pT) distribution across age categories in patients with prostate cancer. White bars represent number of patients with prostate cancer in pT2, while black bars represent patients with prostate cancer in pT3. χ^2 test showed no association between pT and patients age (p=0.621).

TABLE 1
PATHOLOGICAL STAGE ASSOCIATED TO CLINICAL AND PATHOMORPHOLOGICAL PARAMETERS OF THE PATIENTS WITH PROSTATE CANCER

	age (median, range)	PSA (ng/mL) (median, range)	DRE (No)		Gleason score (biopsy) (median, range)	Gleason score (surgical specimen) (median, range)	surgical margin (No)	
			pos	neg			pos	neg
pT2	69 (66–80)	7.5 (2.8–25)	7	60	6 (2–7)	6 (3–7)	18	58
pT3	68 (66–80)	6.4 (5–37.4)	0	16	6 (4–7)	6 (5–9)	11	10
p value	0.275*	0.641*	0.177**		0.235*	0.003*	0.011**	

pos – positive, neg – negative, * Mann-Whitney U-test, ** χ^2 test

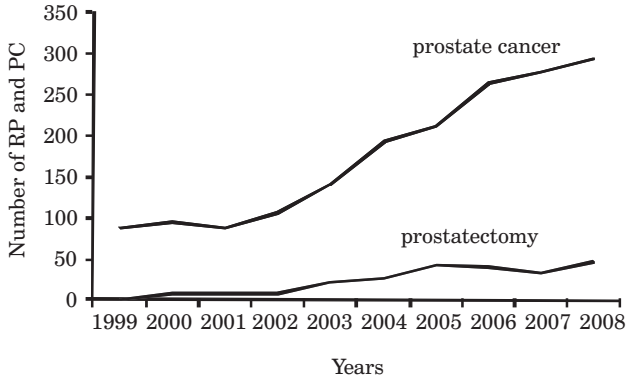

Fig. 2. The number of radical prostatectomy (RP) and prostate cancer (PC) from 1999–2008.

surgery and to positivity of the surgical margins (Table 1). There was no difference in median values of Gleason score between biopsy and surgical specimens. Namely, Gleason score before surgery and that after the surgery showed a significant correlation ($p<0.001$, $r_p=0.475$). Also, Gleason score after the surgery showed a significant association to pT ($p=0.003$), what was not the case for Gleason score of biopsy specimens. We found higher frequency of positive surgical margin in tumors with pT3 (90%) than in pT2 (31%) ($p=0.011$, χ^2 test). Oncological and urological control revealed recurrency of the disease in 8 patients (8.2%). Six of them developed bone metastases, 1 patient had lymph node metastasis and 1 patient developed local recurrency. Total serum PSA in thise patients was less than 10 ng/mL. Five of them were in pT3 group with Gleason score ≤7. All patients but one had tumor with positive surgical margins. Recurrence-free survival was significantly shorter in patients with tumors with positive surgical margins ($p=0.030$ log-rank test) as well as in patients with pT3 stage ($p=0.001$, log-rank test) (Figure 3).

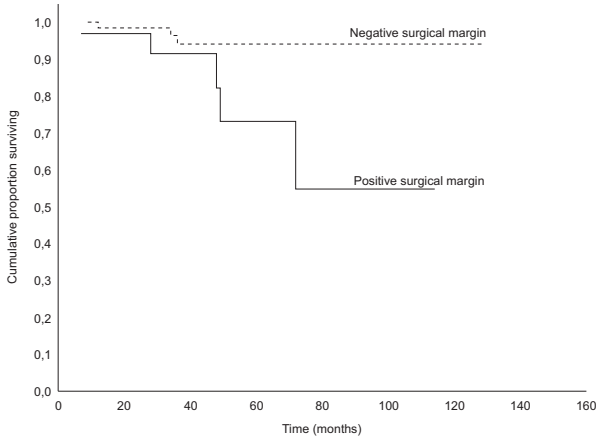

Fig. 3. Recurrence free survival in relation to positive surgical margins status. Kaplan-Meier analysis showed that recurrence-free survival was significantly shorter in patients with tumors with positive surgical margins (p=0.030).

Discussion

Urologists will soon be faced with the reality of a dramatic increase of the elderly and by 2030 the population of men aged ≥65 years is expected to grow up to >71 milion representing 19.6% of the mankind. Modern medicine will prolong life expectancy and according to current dana the average survival of a 70-year-old man is 13 years[13,14]. With the than ageing population, more than 70% of prostate cancer is diagnosed in men aged ≥65 years with significant life expectancy[15]. However, there are still many unanswered questions about the nature and treatment of prostatic carcinoma in this cohort. We could not find a relationship between the age and pT stage as in some previous studies[16,17]. On the contrary, the study of Richstone et. al., found that age ≥70 was associated with extracapsular extension of the tumor and upstaging[14]. PSA testing offers earlier detection of prostatic carcinoma with a lower stage and clinically localized and potentially curable disease by means of aggressive therapy such as prostatectomy[2,18]. This way of treatment substantially reduces the risk of metastasis and symptomatic local tumor growth[19–21]. However, a radical prostatectomy can be done in 10–20% of patients because of late diagnosis of prostatic carcinoma[2]. In our practise the frequency of this procedure is within the mentioned percentage range (13.7%). Low risk criteria for prostatectomy in our population provide an adequate urological and oncological control since we have only 7 patients with progression in metastatic disease and one patient had local tumor progression. The same conclusion was made by Rodriguez et al. suggesting that preoperative PSA values ≤10 ng/mL significantly predict adequacy of this way of treatment as a monotherapy[22]. We did not find significant differences of PSA values between pT2 and pT3 groups of patients yet the mean of preoperative PSA was 7.4 in patients with pT2 tumors and 6.4 ng/mL in a group presenting extraprostatic disease (pT3) with higher maximal values in these patients (range 5–37.4 ng/mL). Almeida et al. in his study showed that patients with prostate confined carcinoma presented significantly lower PSA rates (7.5 ng/mL) in relation to the group of patients with locally advanced disease (12.5 ng/mL)[23]. The same study revealed that patients from group pT2 presented inferior mean values of Gleason when compared to patients in pT3 group as we did in a surgical specimens analysis. Our findings of Gleason score before surgery and that after the surgery showed a significant correlation ($p<0.001$, $r_p=0.475$). The reason could be a shift in Gleason scoring by pathologists over the past decade. Some authors presum that pathologists are more hesitant nowadays to assign low Gleason scores to a diagnostic needle biopsy specimen because low scores are frequently upgraded after a review of the surgical specimen[3,24]. Results of large studies indicated that the positive rate of surgical margin after radical prostatectomy is 20%–40%, and contemporary data suggest that the presence of a positive surgical margin will have an impact on the patient's prognosis[25]. In our study overall positive surgical margin rate was 29.8 % with higher freequency

in pT3 tumors up to 90% what is similar to other studies[26–28]. Recurrence-free survival time was significantly shorter in patients with locally advanced tumors and tumors with positive surgical margins. This is in agreement with the results of Bostwick et al. who found that the impact of a positive margin status on recurrence-free survival appears to be anatomic and site specific[29].

Conclusion

The current data indicated that the presence of positive surgical margins and pT3 stage are useful in the prognosis of a recurrence-free survival period in our group of elderly patients treated with radical prostatectomy.

REFERENCES

1. TAKAHASHI S, SHIRAI T, HASEGAWA R, IMAIDA K, ITO N, Jpn J Clin Oncology, 92 (1992) 117. — 2. HULJEV Ž, Hrvatski časopis za javno zdravstvo, 4 (2008) 1. — 3. ŠPANJOL J, MARIČIĆ A, CICVARIĆ T, VALENČIĆ M, OGUIĆ R, TADIN T, FUČKAR D, BOBINAC M, Coll. Antropol, 1 (2007) 235. — 4. WONG BT, Medical Bulletin, 13 (2008) 17. — 5. KAHEKI Y, JJCO, 33 (2003) 1 — 6. ALBERTSEN PC, HANLEY JA, BARROWS GH, PENSON DF, KOWALCZYK PD, SANDERS MM, FINE J, J Natl Cancer Inst. 97 (2005) 1248. — 7. SMEDLEY HM, SINNOT M, FREEDMAN LS, MACASKILL P, NAYLOR CPE, PILLERS EMK, Br J Urol, 55 (1983) 529. — 8. HOLMBOE ES, CONCATO J, J Gen Intern Med, 15 (2000) 694. — 9. ALIBHAI SM, NAGLIE G, NAM R, TRACHTENBERG J, KRAHN MD, J Clin Oncol, 21 (2003) 3318. — 10. GHVAMIAN R, ZINCKE H, BJU Int, 84 (1999) 160. — 11. AUS G, ABBOU CC, BOLLA M, HEINDEREICH A, SCHMID H-P, POPPEL H, WOLF J, ZATTONI F, Eur Urol 48 (2005) 546. — 12. ORIMO H, ITO H, SUZUKI T, ARAKI A, HOSOI T, SAWABE M, Geriatr Gerontol Int 6 (2002) 149. — 13. RICHSTONE L, BIANCO FR, SHAH HH, KATTANT MW, ESTHAM JA, SCARDINO PT, SHERR DS, BJU International 101 (2002) 541. — 14. MININO AM, SMITH BL, Natl Vital Stat Rep, 49 (2001) 1. — 15. CRAWFORD ED, Urology 62 (2003) 3. — 16. DI MARCO DS, LOHSE CM, BLUTE ML, ZINCKE H, CHEVILLE JS, Urol Oncol 21 (2003) 439. — 17. BOSTWICK DG, QUIAN J, BERGSTTRALH E, J, DUNDORE P, DUGAN J, MYERS JP, J Urol, 155 (1996) 1361. — 18. ZEBIĆ N, ROGGENBUCK U, MANDT D, KRÖPFL D, Coll Antropol 29 (2005) 593. — 19. BILL-AXELSON A, HOLMBERG L, FILÉN F, RUUTU M, GARMO H, BUSCH C, NORDLING S, HÄGGMAN M, ANDERSSON SO, BRATELL S, SPÅNGBERG A, PALMGREN J, ADAMI HO, JOHANSSON JE, N Engl J Med, 352 (2005) 1977. — 20. SCHWARTZ KL, ALIBHAI SM, TOMLISON G, NAGLIE G, KRAHN MD, Urology, 62 (2003) 860. — 21. BUBOLZ T, WASSON JH, LU-YAO G, BARRY MJ, Urology, 58 (2001) 977. — 22. RODRIGUEZ-COVARRUBIAS F, CASTILLEJOS-MOLINA RA, SOTOMAYOR DE ZAVALETA M, GABILONDO-NAVARRO F, FERIA-BERNAL G, Rev Mex Urol, 68 (2008) 273. — 23. ALMEIDA JC, MENESEZ RP, KUCKELHAUS S A, BOCCA AL, FIGUEIREDO F, Int Braz J Urol. 33 (2007) 662. — 24. CHSM DB, HANLON AL, TRONSCO P, AL-SALEEM T, HOROWITZ EM, POLLACK A, Int J Radiat Oncol Biol Phys, 56 (2003) 1241. — 25. YANG Y, Chin Med J, 121 (2008) 375. — 26. SILVA E, FERREIRA U, SILVA DG, MARIANO MB, NETTO NR, BILLIS A, MAGNA LA, Int Urol Nephrol 39 (2007) 865. — 27. WEIDER JA, SOLOWAY MS, J Urol. 160 (1998) 299. — 28. KATZ R SALOMON L, HOZNEK A, TAILLE A, ANTIPHON P, ABBOU CC, J Urol. 169 (2003) 2049. — 29. BLUTE M, BOSTWICK D, BERGSTRALH E, SLEZAK J, MARTIN S, AMLING C, ZINCKE H, Urology 50 (1997) 733.

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PROGNOSTIČKA VRIJEDNOST MORFOLOŠKIH I KLINIČKIH PARAMETARA KOD pT2 – pT3 KARCINOMA PROSTATE U LJUDI STARIJE ŽIVOTNE DOBI

SAŽETAK

Karcinom prostate je bolest starije životne dobi, čija incidencija raste s godinama. Ova studija prikazuje povezanost između kliničkih i morfoloških parametara u lokalno ograničenom (pT2) i lokalno uznapredovalom (pT3) stadiju karcinoma prostate. Analizirali smo grupu ljudi starije životne dobi u kojih je učinjena radikalna prostatektomija u razdoblju između 1999. i 2008. u KBC Rijeka. Nismo našli statistički značajnu povezanost između pT stadija te starosti bolesnika, prijeoperacijske vrijednosti prostata specifičnog antigena, digitorektalnog pregleda i Gleason zbroja dobivenog biopsijom. Statistički je prisutna značajna povezanost između većeg Gleason zbroja u uzorcima radikalne prostatektomije kao i veća učestalost pozitivnih kirurških rubova u tumora pT3 stadija nego pT2 (p=0.003; p=0.011). Razdoblje bez znakova povratka bolesti je bio kraći u bolesnika s pozitivnim kirurškim rubovima kao i u bolesnika s pT3 stadijem (p=0.030; p=0.001). Možemo zaključiti da su tumori višeg stadija kao i prisutnost pozitivnih kirurških rubova pokazatelj lošije prognoze u naših pacijenata.