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# Validation of Epstein Biopsy Criteria for Insignificant Prostate Cancer in Contemporary Cohort of Croatian Patients

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**ABSTRACT**

*Only few reports validated contemporary Epstein criteria for insignificant prostate cancer, and only one being from Europe. Patients with insignificant prostate cancer should be offered active surveillance and spared radical treatment. In our study we tested Epstein biopsy criteria for predicting unfavorable final pathology and biochemical relapse in low risk prostate cancer patients, who were eligible for active surveillance but where treated with radical prostatectomy. Between January 2003 and January 2008, 586 patients were subjected to radical prostatectomy in our institution. Among them, 106 where eligible for active surveillance according to Epstein biopsy criteria for insignificant prostate cancer. We analyzed the presence of adverse pathological findings in the final pathohistological specimen after radical prostatectomy which excludes low risk disease. Adverse pathohistological findings were noted in 41 (38.6%) patients, who could have been offered active surveillance. During the follow up of 48 (12 – 72) months, biochemical relapse was noted in 6 (5.6%) patients. Although active surveillance is becoming more popular because of the long natural course of prostate cancer and fear of overtreatment of patients with indolent course of disease, both doctors and patients must be aware of potentially significant disease in this group and limitations of current preoperative criteria defining low risk patients.*

***Key words:*** *active surveillance, prostate cancer, low – risk prostate cancer, radical prostatectomy*

## Introduction

Insignificant prostate cancer is defined as a biologically indolent disease that poses no threat to the patient´s life[1]. Due to wide use of prostate specific antigen (PSA), stage and grade migration towards low stage, low volume disease is noted. Fear of over diagnosis and overtreatment of indolent prostate cancer raised the question of optimal treatment of early prostate cancer. Active surveillance is a legitimate option for treatment of low risk, localized prostate cancer[2]. It includes an active decision not to treat patients immediately, but to follow them with a surveillance protocol and to treat them at predefined thresholds that classify progression of the disease (short PSA doubling time and deteriorating histopathological factors on repeat biopsy) while the disease is still curable[3]. The aim of active surveillance is to reduce the overtreatment in patients with organ confined low risk prostate cancer, without giving up radical treatment for those who need it. In later cases, the definitive treatment should be curative. There are several groups of criteria defining low risk prostate cancer eligible for AS (e.g. clinically confined prostate cancer (p T1-T2), Gleason score $\leq$7, PSA <15 – 20 ng/ml)[4,5]. In our study we tested Epstein biopsy criteria for predicting unfavorable final pathology and biochemical relapse in the group of low risk prostate cancer patients, who were eligible for active surveillance but where treated with radical prostatectomy.

## Material and Methods

From January 2003 until January 2008, in our institution 586 patients were subjected to retropubic radical prostatectomy. Among them, 106 patients were eligible for active surveillance under preoperative biopsy criteria de-

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fined by Epstein. These criteria imply clinical stage T1c – T2, PSA density <0.15 ng/ml/ml, biopsy Gleason score ≤3+3, ≤2 positive biopsy cores, ≤50% involvement by cancer in any single core. Data were obtained from a prospectively maintained database of patients who were biopsied and operated in our institution. Both preoperative and postoperative serum PSA were obtained in our institution using the same kit. The biopsy and radical prostatectomy specimens were processed using standard fixation protocol and were evaluated by two uropathologists. PSA density was calculated using preoperative PSA divided by measured volume of the prostate in the radical prostatectomy specimen since preoperative transrectal ultrasound volume was not available for all patients. We analyzed presence of the adverse pathological findings in the final pathohistological specimen after radical prostatectomy which exclude low risk disease: presence of extracapsular spread of the disease (ECE), positive surgical margins (+SM), affectedness of the seminal vesicle (+ SV), positive lymph nodes (PLN) and Gleason score 7 – 10.

### *Statistical analysis*

Data were described as frequency tables. Analysis was performed using StatView 5.0 (SAS Institute Inc, Cary, NC, USA). Statistical significance was set at p<0.05%.

## Results

From 586 patients treated with radical prostatectomy in the analyzed period, 106 belonged to the low – risk group of patients for the above preoperative criteria and could be subjected to active surveillance. Mean age was 65 (46 – 7) year, mean PSA was 7.1 (3.0 – 10.0) ng/mL, mean biopsy Gleason score was 5.8 (4 – 6), mean number of biopsy core was 8 (6 – 12), mean percent of tumor in core was 18 (5 – 50)%. Among them ECE, + SM, SVI were found in 6.6%, 8.4% and 1.8% patients, respectively. Gleason score 7 was noted in 39 patients in the final pathohistological report, and Gleason score 8 – 10 in none. Total, adverse pathohistological finding was noted in 41 patients, which was 38.6% of all patients that could be offered active surveillance. During the follow – up of 48 (12 – 72) months biochemical relapse was noted in 6 patients.

## Discussion

Prostate cancer is accounted for 14% of new male cancers in Croatia in 2006[6]. Cancer – specific 10 – year survival rates for stage T1a patients is 96% and 94%, for well and good differentiated tumours[7]. The metastasis – free 10 – year survival rate was 92% for patients with well, but 78% for those with good differentiated tumours[7]. The 15 year risk of dying from prostate cancer in relation to Gleason score at diagnosis in patients with localized disease aged 55 – 74 years is, for Gleason score 5, 6 and 7, 6 – 11%, 18-30% and 42 – 70%, respectively[8,9]. In our study, we tried to reevaluate current criteria for enrolling presumably low – risk prostate cancer patients to active surveillance. We used the most stringent criteria according to the literature[8,9]. In our group of patients with presumably low – risk prostate cancer according to established criteria, 38.6% had adverse pathohistological findings, and 5.6% had biochemical relapses after the operation they were subjected to.

## Conclusion

Although active surveillance is becoming more popular because of the long natural course of prostate cancer and fear of overtreatment patients with indolent course of disease, both doctors and patients must be aware of potentially significant disease in this group and limitations of current preoperative criteria defining low – risk patients.

## REFERENCES

1. KLEIN EA, Cancer, 101 (2004) 1923. DOI: 10.1002/cncr.20584. – 2. BASTIAN PJ, MANGOLD LA, EPSTEIN JI, PARTIN AW, Cancer, 101 (2004) 2001. DOI: 10.1002/cncr.20586. – 3. KLOTZ L, JCO, 32 (2005) 8165. DOI: 10.1200/JCO.2005.03.3134. – 4. HEIDENREICH A, AUS G, BOLLA M, JONIAU S, MATVEEV V, SCHMID HP, ZATTONI F, Eur Urol, 53 (2008) 68. DOI: 10.1016/j.eururo.2007.09.002. – 5. ADOLFSSON J, BJU Int, 102 (2008) 10. DOI: 10.1111/j.1464-410X.2008.07585.x. – 6. Latest data Of Cancer monitoring with a registry, Croatian Institute of Public Health, accessed 29.07.2013, Available from: URL: http://www.hzjz.hr/rak/novo.htm. – 7. CHODAK GW, THISTED RA, GERBER GS, JOHANSSON JE, ADOLFSSON J, JONES GW, CHISHOLM GD, MOSKOVITZ B, LIVNE PM, WARNER J, N Engl J Med, 330 (1994) 220. DOI: 10.1056/NEJM199401273300403. – 8. ALBERTSEN PC, HENLEY JA, GLEASON DF, BARRY MJ, JAMA, 280 (1998) 975. DOI: 10.1001/jama.280.11.975. – 9. ALBERTSEN PC, HENLEY JA, MURPHY SM, J Urol, 162 (1999) 439. DOI: 10.1016/S0022-5347(05)68580-1.

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## PATOHISTOLOŠKI NALAZI BOLESNIKA S RAKOM PROSTATE LIJEČENIH RADIKALNOM PROSTATEKTOMIJOM KOJI SU BILI PODOBNI ZA AKTIVNI NADZOR


### S A Ž E T A K

Samo je nekoliko radova koji potvrđuju Epsteinove kriterije za karcinome prostate niskog rizika od kojih je samo jedan iz Europe. Aktivni nadzor je legitimna opcija kod lokaliziranog karcinoma prostate niskog rizika. U našem istraživanju testirali smo u skupini bolesnika niskog rizika, koja je liječena radikalnom prostatektomijom, najstrože preoperativne kriterije za aktivni nadzor. Od siječnja 2003. do siječnja 2008. retropubičnoj radikalnoj prostatektomiji podvrgnuto je 586 bolesnika od kojih je 106 bilo podobno za aktivni nadzor prema kombiniranim preoperativnim kriterijima koje su definirali van den Bergh i Carter. Analizirali smo prisutnost nepovoljnih patoloških nalaza na konačnom patohistološkom preparatu nakon prostatektomije koji isključuju bolest niskog rizika. Ukupno, nepovoljan patohistološki nalaz bio je prisutan u 41 bolesnika, što je 38,6% bolesnika kojima je mogao biti ponuđen i aktivni nadzor. Tijekom perioda praćenja od 48 (12-72) mjeseci biokemijski relaps zabilježen je u 6 bolesnika. Premda aktivni nadzor postaje popularan zbog dugog prirodnog tijeka raka prostate i straha od pretjeranog liječenja bolesnika sa indolentnim tijekom bolesti i liječnici i bolesnici moraju biti svjesni potencijalno signifikatne bolesti u ovoj skupini i ograničenja sadašnjih preoperativnih kriterija koji definiraju bolesnike niskog rizika.