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DIAGNOSTIC VALUE OF SERUM PROSTATE-SPECIFIC ANTIGEN IN PATIENTS WITH POTENTIALLY CURABLE PROSTATIC CARCINOMA

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The aim of the paper was to analyze the age structure of patients in whom early diagnosis of prostatic carcinoma was performed. Diagnostic values of total PSA and age-specific PSA were compared.

One hundred patients (mean age 67 years) with the negative digital rectal examination and serum PSA levels 4 ng/ml-10 ng/ml were analyzed. In all patients transrectal ultrasound guided biopsy (12 biopsy cores) was performed. Serum PSA was measured in the control group as well. Control group consisted of 100 age-matched males (mean age 66), with the good overall health state -human blood donors, with the negative digital rectal examination and PSA levels below 4 ng/ml. Age-specific PSA was analyzed in both groups.

PSA was significantly different in patients with benign prostatic hyperplasia compared to the patients with prostatic carcinoma. There was no difference between the PSA and age-specific PSA. Sensitivity and specifity of the age-specific PSA referral range was 92.3% and 16.4%, respectively.

Principles of early detection of the prostatic carcinoma were not necessary in 38% of patients. They were not the target population for the early diagnosis of the prostatic carcinoma. Unnecessary prostate biopsies could be reduced up to 16%, using the age-specific PSA. Prostatic carcinoma would be missed in 7.6% of patients. False positive biopsy rate in patients within the referral range of the age specific PSA was 83.8%, so the question remains how the number of unnecessary prostate biopsies could be reduced. *Acta Medica Medianae 2017;56(1):5-8.*

Key words: *antigen, prostate, specific*

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Introduction

Prostatic carcinoma is a fourth cancer in line regarding the incidence of malignancy in Serbia (after bronchial, colorectal and ventricular carcinoma). Annual incidence of the prostatic carcinoma rose up to 82%, between the years 1968 and 2000.

Prostate specific antigen (PSA) is ranked among the most valuable tumor markers in early detection, staging, follow-up and the evaluation of the treatment of the prostatic carcinoma. Different measurements of total PSA were used in order to improve its specificity (PSA density, PSA velocity, percentage of total and free PSA and the age-specific ranges of PSA) (1, 2).

There is an evidence that continual increase of the prostatic size with ageing is followed by the simultaneous changes of PSA, so, it became obligatory to define age-specific ranges of the normal PSA in order to improve sensitivity and specificity of PSA testing (3, 4).

It is mandatory to define the program of early diagnosis of the potentially curable prostatic carcinoma (pT1-pT2). Analysis of the biopsy material confirmed a high frequency of the negative findings especially in patients with PSA values between 4-10 ng/ml (grey zone), and negative digital rectal examination (5-7).

The aim of the study is to investigate the importance of age-specific ranges of PSA.

Material and methods

One hundred patients (ages between 46 and 85) with the negative digital rectal examination were evaluated between April 2010 and September 2011. PSA was obtained before and 30 days

after the digital rectal examination and processed using Tandem R assay. PSA values lower than 4 ng/ml and higher than 10 ng/ml were recorded in 70 patients. In 30 patients, PSA was 4-10 ng/ml.

Patients with the positive digital rectal examination (DRE), previously confirmed prostatic carcinoma and patients with the previous medical or surgical treatment of benign prostatic hyperplasia were not included in the study.

Prostate biopsy was performed in a standard manner in 30 patients with the PSA between 4-10 ng/ml and suspected malignancy (6-12 biopsy cores).

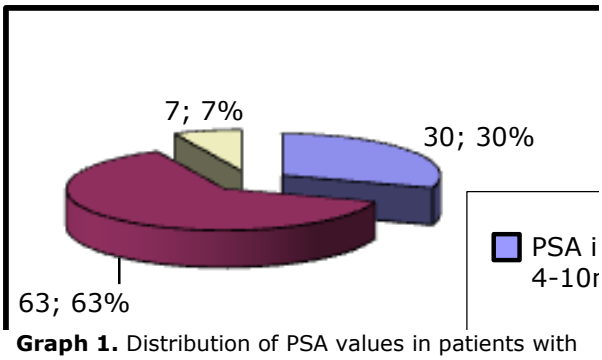
Age-specific PSA was also evaluated. Age-specific ranges of PSA were 2.5 ng/ml, 3.5 ng/ml, 4.5 ng/ml and 6.5 ng/ml for the age ranges 40-49, 50-59, 60-69, and 70-79, respectively.

In all patients, disease history, DRE, general examination, blood analysis, transrectal ultrasound of the prostate with the prostate size measurement were performed. Blood levels of total and free PSA were analyzed as well as the age-specific PSA.

Statistical evaluation was performed with the Student's t-test, Man-Whitney test, sensitivity and specifity.

Results

Total PSA below 4 ng/ml was recorded in 63/100 (63%) patients. PSA over 10 ng/ml were recorded in 7/100(7%) patients. Total PSA 4-10 ng/ml was recorded 30/100 (30%) patients (Graph 1). Lower urinary tract symptoms were the main complaint in 78/100 (78%) patients. Twenty -two 22/100 (22%) patients were asymptomatic, periodical health state test was self-requested.



Graph 1. Distribution of PSA values in patients with negative digital rectal examination

Statistical correlation of total and the age-specific PSA

Diagnostic value of the age-specific PSA was compared in patients with the urinary symptoms (range 57-87; mean age 67 years) and asymptomatic patients (range 46-68, mean age 66 years) (Mann Whitney p <0.001).

Prostatic carcinoma was confirmed in 5/30 (16.6%) patients with the PSA level 4-10 ng/ml and negative DRE. In 25 (83.4%) patients, benign prostatic hyperplasia was present.

PSA was 4.43-9.63 ng/ml (mean 7.71) in patients with prostatic carcinoma. PSA was 4.28-9.63 ng/ml (mean 6.63) in patients with BPH (T test p = 0.007).

Age-specific PSA was increased in 4/20 (80%) patients with the prostatic carcinoma, and in 21/25 (84%) patients with the negative prostate biopsy, so, the sensitivity of the age-specific PSA was 90% and specificity was 16%.

Discussion

There is evidence that there is a continual increase of PSA in males with BPH. Therefore, the age-matched referral values need to be applied. Total PSA was significantly different in the investigated compared to the control group. Consequently, the number of the potentially curable prostate carcinoma especially in younger patients is increased (9).

Asymptomatic patients were significantly younger than patients with lower urinary tract symptoms (p = 0.001). Our satisfaction was incomplete because of only 22% self-initiated PSA controls. Quite the contrary, 38.07% of the patients were older than 70, in whom potentially curable treatment is not an option (10).

Our opinion is that the principles of early detection of the prostatic carcinoma are useless in patients who are not eligible for the curative treatment. Our result suggests that continual education should be improved through the program of early detection of the prostatic carcinoma in younger asymptomatic patients who are eligible for the radical treatment. Experiences in Britain are favorable, especially in the education of the lower social classes (11).

PSA was significantly different in patients with the prostatic carcinoma compared to the patients with BPH, negative DRE and PSA 4-10 ng/ml (t-Test p = 0.007) (12). There is a high incidence of negative (unnecessary) prostate biopsies. Therefore, age-matched PSA, a simple, non-expensive test, should not be missed by the medical practice in Serbia.

Interpretation of the age-specific referral values of PSA in everyday urological practice is important for making an indication for the prostate biopsy. Our results confirm that there are not statistically significant differences of the age-related PSA compared to PSA. Age-related PSA test has a diagnostic sensitivity of 92.3%, however, 7% of the prostatic carcinoma are missed.

Percentage of false negative results (7.7%) suggests that early diagnosis of the prostatic carcinoma should be practiced. It could be solved with the regular annual examinations. Mettlin reports a low sensitivity (67.3%) of PSA in his paper (13).

Our results demonstrate that specificity of the age-related PSA is 16.4%. The total number of prostate biopsies was reduced in 16.4% compared to PSA without the influence on test sensitivity. Catalona has previously reported reduction of the number biopsies in 15% of patients, and 8% of

the missed prostatic carcinoma (14). Diagnostic value of the age-related PSA in patients with the prostatic carcinoma is confirmed by the reduction of the prostate biopsies up to 21%, in patients over 60, and 4% of the missed organ-confined prostatic carcinomas (15).

There is also evidence that there are race-specific differences of PSA. Age-related referral PSA values should be defined in every ethnic group (16).

Total/free PSA and PSA density contributed to the reduction of unnecessary prostate biopsies (19% - 95%) (17, 18). EAU guidelines suggests repeated prostate biopsies in patients with the permanent indication for the prostate biopsy regardless of negative prior biopsies. Keetch reports that 20% of prostate carcinomas are detected in repeated prostate biopsies (19). However, prostate biopsies should be repeated in patients with both high grade prostatic intraepithelial neoplasia and atypical small cell proliferation. In our opinion, there are existing opposite tendencies between our wish to reduce the number of unnecessary prostate biopsies and repeated biopsies in patients with the first negative biopsy. A thorough follow-up is suggested in patients with negative DRE and total PSA values ranging from 4 to 9.9 ng/ml.

Conclusion

In conclusion, age-related PSA reduced the number of prostate biopsies by 16%, but overlooked 8% of patients with prostatic carcinoma. There is no suggestion to perform PSA test in the general population over the specific age limit.

It is also necessary to compare the diagnostic value of the age-specific PSA and compare to the other modalities of PSA measurement, such as PSA density and total/free PSA.

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DIJAGNOSTIČKA VREDNOST SERUMSKOG PROSTATE-SPECIFIČNOG ANTIGENA KOD MUŠKARACA ODREĐENE STAROSNE STRUKTURE U CILJU RANOG OTKRIVANJA KURABILNOG KARCINOMA PROSTATE

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Cilj rada bio je analizirati starosnu strukturu populacije kod koje se sprovodi rana dijagnostika karcinoma prostate i uporediti dijagnostičku vrednost serumskog prostate-specifičnog antigena (PSA) i starosno-zavisnog PSA koji je specifičan za godine bolesnika u razlikovanju karcinoma prostate i benigne hiperplazije prostate. Ispitivano je 100 muškaraca prosečne starosti 67 godina koji su imali negativan digitorektalni nalaz i nivo serumskog PSA od 4,0-10 ng/ml. Kod svih 100 muškaraca koji su imali nivo serumskog PSA od 4,0-10,0 ng/ml učinjena je biopsija prostate pod kontrolom transrektalnog ultrazvuka uzimajući najmanje 12 biopsijskih uzoraka. Nivo serumskog PSA meren je i kod kontrolne grupe koju je činilo 100 muškaraca, redovno zdravstveno testiranih (dobrovoljnih davaoca krvi), sa prosekom godina 66, koji su imali negativan digitorektalni nalaz i PSA ispod 4 ng/ml. Kod obe grupe su se analizirale vrednosti starosno zavisnog PSA. Vrednost serumskog PSA kod obolelih od benigne hiperplazije prostate su se značajno razlikovale od vrednosti PSA kod bolesnika kod kojih je dokazan karcinom prostate. Nije bilo razlike između vrednosti serumskog PSA i referentnog raspona PSA koji je specifičan za godine. Osetljivost referentnog raspona PSA koji je specifičan za godine bila je 92,3%, a njegova specifičnost 16,4%. Principi rane dijagnostike sprovode se nepotrebno kod čak 38% ispitanika koji ne predstavljaju ciljnu populaciju za ranu dijagnostiku. Takođe, služeći se kriterijumima referentnog raspona PSA koji je specifičan za godine, može se smanjiti broj nepotrebnih biopsija za 16,4% dok se dokazivanje karcinoma prostate propušta u 7,6% slučajeva. Procenat lažno pozitivnih nalaza referentnog raspona PSA koji je specifičan za godine je 83,58%, pa se sa razlogom postavlja pitanje nalaženja načina za smanjenje broja nepotrebnih biopsija. Acta Medica Medianae 2017;56(1):5-8.

Ključne reči: *antigen, prostata, specifičan*