Improved Discrimination of Prostate Cancer and Benign Prostatic Hyperplasia by Means of the Quotient of Free and Total PSA

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The value of t-PSA (total prostate specific antigen) and of the quotient of free and t-PSA (% f-PSA) for the discrimination of BPH (benign prostatic hyperplasia) and PC (prostate cancer) as well as possible influencing factors were subject to examination under study conditions.

The sera of 210 patients (131 BPH, 79 PC patients) were examined by means of the Immulite® test; thereof 76 male patients (47 BPH, 29 PC patients) were found to have a t-PSA-value between 4 and 10 ng/ml (grey area).

Apart from the age and the findings of rectal digital examination, we recorded the prostate volume, indications of non-specific increases in PSA and for PC patients also the TNM-G stage.

For patients with prostate cancer the quotient of f- and t-PSA was significantly lower (median: 0.08) than compared to patients with BPH (median: 0.22) (p<0.001). Also in the grey area the quotient was significantly lower in patients with malignant diagnosis (median: 0.12) than for patients with a non-malignant diagnosis (median: 0.21) (p<0.001).

ROC curves were prepared in order to compare the capability of discrimination of the two parameters. At this point, the better discrimination potential of the quotient in the grey area became evident. Due to the fact that priority was given to the detection of carcinoma, the threshold value was defined at a level at which high sensitivity (90%) is existent in combination with an acceptable specificity (approx. 50%). The resultant values are for the total PSA area 0.21, for the grey area 0.19 as a cut-off.

Neither the age, nor the prostate volume, nor urinary tract infections had any influence upon the quotient. There was also no correlation between the stage or the grading of the tumour and the percentage of the f-PSA.

The quotient alleviates the discrimination between BPH and PC, in particular in the diagnostically problematic grey area. Thus, it can serve as an aid for the decision "biopsy or re-biopsy". As there is currently no standardized method for the application of % f-PSA, there is a requirement for further examination under homogeneous criteria.

Introduction

PSA as a sperm marker was initially confined to legal medicine but has since become an important parameter for the diagnosis and therapy control of prostate cancer. The grey area in the t-PSA values between 4 and 10 ng/ml remains to be problematic. In this area, benign as well as malignant alterations of the prostate are seen. Prostate cancer is often limited to the organ itself.
Different concepts have been developed in order to improve the discrimination between non-malignant and malignant diseases. These concepts are subject to controversial discussion: PSA density, transitional zone density and PSA velocity. Age-specific threshold values for t-PSA appear to be very promising (PSA aging).

New perspectives have been opened through the detection of different PSA isomers by Scandinavian biochemists.

In this study the subject of examination was the value of the quotient of free PSA (f-PSA) and total PSA (t-PSA) for the discrimination between benign prostatic hyperplasia (BPH) and prostate cancer (PC). At the same time, the correlation between the quotient and possible influencing factors was investigated.

Patients and methods

Patients: In a prospective study the f- and t-PSA were determined in 131 BPH and 79 PC patients. Of these, 76 men (47 BPH, 29 PC patients) had a t-PSA value in the grey area. Apart from the age and the findings of digital rectal examination, the prostate volume as well as indicators of non-specific PSA changes (urinary tract infection, prostatitis, finasteride) were recorded, in cases of prostate cancer also the TNM-G stage. For securing of the diagnosis six random biopsies of the prostate were performed in all patients. In patients with carcinoma pelvic lymphadenectomy and radical prostatectomy were additionally carried out. In 17 men a hormone withdrawal had taken place before radical prostatectomy by application of antiandrogens and/or Gn-RH analogues.

Determination of PSA: f- and t-PSA were determined by means of the Immulite® test. Blood was drawn before rectal examination and at least 6 weeks after prostate surgery. Blood specimens not immediately worked upon were frozen at −20 °C.

Statistics: A χ² adjustment test was carried out for the verification of the standard distribution. In instances of too small random tests the data underwent a Kolmogoroff–Smirnov adjustment test. Due to the fact that the values for f-PSA and t-PSA did not follow the standard distribution, although the random test specimens were to be considered as independent, the differences in the central tendency were examined by means of a U-test. ROC curves were set up for testing the potential of discrimination of total PSA and % f-PSA. The correlation of age, prostate volume, infection, TNM-G stage and PSA-quotient was examined. An analysis of the reaction of the quotient on the respective factors for both groups of patients pertinent to the total PSA and the PSA grey area served as a basis for that examination.

A simple linear regression was applied for age and prostate volume. The question as to whether there is a correlation between an infection (UTI, prostatitis), a locally limited or advanced prostate cancer and between the quotient was investigated upon by means of a U-test. The Kruskal–Wallis test served