Molecular Forms of Prostate-specific Antigen in Malignant and Benign Prostatic Tissue: Biochemical and Diagnostic Implications

Klaus Jung,1* Brigitte Brux,2 Michael Lein,1 Birgit Rudolph,3 Glen Kristiansen,3 Steffen Hauptmann,3 Dietmar Schnorr,1 Stefan A. Loening,1 and Pranav Sinha2

Background: Patients with prostate cancer (PCa) show a lower ratio of free prostate-specific antigen (fPSA) to total PSA (tPSA) in serum than patients with benign prostatic hyperplasia (BPH). The patterns of the intracellular PSA isoforms in malignant and benign prostatic tissue have been studied as potential molecular reasons for this phenomenon.

Methods: Prostatic tissue samples were obtained after cystoprostatectomy from patients with bladder cancer (n = 10), from BPH patients (transurethral resection of the prostate, n = 10; adenomectomy, n = 10), and from the cancerous and noncancerous parts of the same prostates removed surgically by prostatectomy because of PCa (n = 20). PSA pattern was characterized by gel filtration, immunoblotting, and immunoassays for tPSA, fPSA, α1-antichymotrypsin-PSA (ACT-PSA), and complexed PSA (Bayer Immuno 1 assay). Comparisons were made with the PSA concentrations in serum.

Results: The major portion of tPSA in all tissue samples was fPSA; complexed PSA forms were <2%. Samples from cystoprostatectomy patients had the lowest and those from adenomectomy patients the highest values of tPSA and fPSA. PSA concentrations were lower in cancerous than in the noncancerous parts of the prostate. No significant correlations were found between tumor stage or grade and the amounts of tPSA, fPSA, and ACT-PSA in tissue. Tissue PSA values were not correlated with the serum PSA concentrations nor with the ratios fPSA/tPSA and ACT-PSA/tPSA in sera.

Conclusions: The amounts of tPSA and the PSA isoforms in prostatic tissue explain neither the concentrations of tPSA and PSA isoforms in serum nor the behavior of the ratio fPSA/tPSA in patients with BPH and PCa.

© 2000 American Association for Clinical Chemistry

Prostate-specific antigen (PSA)4 occurs in serum in different molecular forms (1, 2). Approximately 70–90% of the total PSA (tPSA) is bound to α1-antichymotrypsin (ACT), and a small amount is complexed with α1-antitrypsin and protein C. The portion of PSA that is complexed with α2-macroglobulin can be measured only if the complex is cleaved and the PSA epitopes become accessible. Free PSA (fPSA), the portion of PSA not bound to serum proteins, accounts for 10–30% of tPSA. A lower ratio of fPSA to tPSA (fPSA/tPSA) in patients with prostate cancer (PCa) has been demonstrated in numerous studies [reviewed in Ref. (3)]. This ratio has been considered as a helpful tool for distinguishing between PCa and benign prostatic hyperplasia (BPH).

Several factors that influence the ratio fPSA/tPSA in serum, e.g., age, prostate size, drug treatment, prostate manipulation, sample stability, or assay method, have been reviewed recently (4, 5). However, the reason for the changed ratio in PCa patients has not yet been clarified on a molecular basis, although some hypotheses exist (6).

Thus, the reduced ratio may be attributable to differences at the cellular level: (a) a changed synthesis of ACT in neoplastic cells compared with benign cells (7), leading to increased formation of ACT-PSA complex early in malignant cells before release into circulation; (b) the release of different proportions of enzymatically inactive PSA that react differently with ACT in the circulation (6, 8); and (c)
the alteration of the glycosylation rate of PSA in neoplastic cells, leading to characteristic differences of the elimination kinetics of the PSA isoforms from blood (9).

Because these models have not been clarified in detail, our investigation had three objectives: (a) to assess the pattern of the main intracellular PSA isoforms in both malignant and benign prostatic tissue, using various biochemical techniques; (b) to evaluate the relationships between the intracellular PSA pattern and the occurrence of the serum PSA isoforms in patients with PCa and BPH; and (c) to infer from these results whether the intracellular PSA pattern determines the typical fPSA/tPSA ratio in serum of patients with PCa and BPH.

Materials and Methods

STUDY GROUPS AND SAMPLES

The use of tissue and blood samples for research purposes was approved by the Human Use Committee of the Charité Hospital, Berlin.

Groups investigated. A total of 50 men were studied, including a group of 10 men (median age, 61 years; range, 44–72 years) undergoing cystoprostatectomy for bladder cancer with a histologically confirmed absence of PCa (group CYS), 20 patients with BPH (median age, 71 years; range, 63–81 years), and 20 with PCa (median age, 65 years; range, 57–71 years). Ten of the BPH patients underwent transurethral resection of the prostate (group TUR-P), and 10 had open adenomectomies (group ADE). Each PCa patient had been classified according to the TNM system, and the histological grade had been classified as grade 1, 2, or 3. The number of patients in each classification according to pathological stages and grades were as follows: pT2 pN0M0, n = 14; pT3 pN0M0, n = 6; G1, n = 2; G2, n = 14; and G3, n = 4.

Blood samples. Blood samples were taken before diagnostic procedures of the prostate or 4 weeks (at the earliest) after digital rectal examination, prostatic biopsy, and transrectal ultrasound. The samples were collected in evacuated tubes (Monovette 03.1528; Sarstedt GmbH) and were centrifuged at 1600g for 15 min at 4 °C after the blood had clotted for 1 h at room temperature. The sera were frozen at −80 °C within 2 h after collection and were not thawed (and refrozen) before being tested within 12 weeks.

Tissue samples. Prostate tissue samples were obtained from the cancerous and noncancerous parts of the same prostate that had been surgically removed by radical prostatectomy so that matched pairs were used. Small pieces of tissue were dissected immediately after removal of the prostate and stored in liquid nitrogen until analysis. The cut edges within the prostate were inked so that the dissected pieces could easily be assigned to the adjacent prostate tissue examined histopathologically. Similarly, prostate tissue material from cystoprostatectomies, adenomectomies, and transurethral resections were collected. Histological analysis from all tissue pieces used was performed by clinical pathologists (B.R. and G.K.) as described previously in detail to ensure that the material used was either malignant or nonmalignant tissue (4).

Preparation of tissue extracts. Tissue samples (~30–50 mg) were thawed, cut into small pieces, and homogenized in 100 μL of 10 mmol/L sodium phosphate buffer, pH 7.46, containing 2.5 mL/L Triton X-100 with a Wheaton glass homogenizer by 10 strokes on ice and were additionally sonicated. The homogenate was transferred into a 1.5-mL tube (Eppendorf GmbH). The homogenizer was rinsed twice with 100 μL of Triton solution. This mixture of 300 μL was centrifuged at 23,000g for 15 min at 4 °C. The supernatant was removed. To investigate the effect of the extraction procedure, the pellet was resuspended and the extraction was repeated several times. The recommended final extraction procedure consisted of three extractions with Triton solution and the measurements of the analytes in the combined supernatants. All supernatants were stored at −80 °C until analysis.

Additional samples investigated. To compare the results obtained with samples described in the study groups, the following specimens were used: a serum with high PSA concentration (2170 μg/L) from a patient with advanced PCa; seminal plasma; and purified PSA from human seminal fluid (Calbiochem-Novabiochem) incubated at 37 °C for 3 h with either 50 mmol/L phosphate buffer, pH 7.4, containing 50 g/L human serum albumin (Serva Feinbiochemica) or with a female serum pool. All samples were stored at −80 °C until used.

PROCEDURES

Immunoassays for PSA. As indicated in the text, tPSA was measured with the Roche Elecsys PSA Immunoassay (Roche Diagnostics), the IMMULITE PSA assay (Diagnostic Products), the AxSYM PSA assay (Abbott Diagnostics), or the Bayer Immuno 1 PSA Assay (Bayer Diagnostics). fPSA was measured with the IMMULITE Free PSA kit, the Roche Elecsys Free PSA Immunoassay, or the AxSYM Free PSA assay. According to the information provided by the manufacturers, all tests are equimolar assays for determining PSA. To measure complexed PSA (cPSA), a recently introduced immunoassay (product no. T01-3982-51; Bayer Diagnostics) for the Bayer Immuno 1 system was used (10). This assay is based on the unique binding properties of the capture monoclonal antibody MM1 used in the Bayer Immuno 1 assay for tPSA. That antibody fails to bind fPSA in the presence of specific antibodies against epitope E, which is exposed only in fPSA, so that all cPSA forms such ACT-PSA and minor forms except PSA complexed to α2-macroglobulin are detected.

To measure ACT-PSA, two prototype assays on the ES immunoanalyzer (Roche Diagnostics) were used. The principle of the tests was described previously and is based on the two-step sandwich technique (11). Samples
are incubated in the first step with specific monoclonal biotinylated antibodies, forming a PSA-antibody sandwich complex that is bound by the biotinylated antibodies to the streptavidin-coated tubes. After washing, an horseradish peroxidase-labeled mouse anti-ACT conjugate for determining ACT-PSA is added and bound to the PSA-antibody complex in a second incubation cycle. The two assays differed in the use of different antibodies. After incubation, the tubes are emptied and washed. The substrate diammonium 2,2′-azino-bis(3-ethyl-benzothiazoline-6-sulfonate) is then added, and the absorbance is measured after 30 min.

To measure PSA and its isoforms in tissue extracts, the supernatants were removed from the freezer and thawed by agitation at room temperature. Necessary dilutions were made either with 50 mmol/L phosphate buffer, pH 7.4, containing 50 g/L human serum albumin or with special dilution solutions supplied with the corresponding test kits.

**Gel filtration chromatography.** Samples containing 1.3–2.5 μg of tPSA were loaded on a Sephacryl S-200 column (1.6 × 90 cm; Pharmacia) and eluted with 20 mmol/L phosphate buffer, pH 7.4, containing 50 mmol/L NaCl and 5 mmol/L NaN3 at a flow rate of 9.6 mL/h. Fractions containing 1.3–2.5 mg/mL phosphate buffer, pH 7.4, containing 150 mmol/L NaCl and 5 mmol/L NaN3 at a flow rate of 9.6 mL/h. Fractions (1.6-mL) were collected, aliquoted, and stored at −80 °C until analysis within 12 weeks. The column was calibrated with ferritin (450 kDa), catalase (240 kDa), bovine serum albumin (65 kDa), egg albumin (45 kDa), chymotrypsinogen A (25 kDa), and equine myoglobin (17.8 kDa) by measuring the absorbance at 280 nm in the fractions.

**Electrophoresis and immunoblotting.** Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) was performed under reducing conditions on the Mini Electrophoresis Unit 2050 (LKB) according to the standard method of Laemmli (12). Samples heated at 95 °C for 5 min in sample buffer containing 50 mL/L 2-mercaptoethanol and 20 g/L SDS were applied to a 4% stacking gel and electrophoresed through a 10% SDS polyacrylamide gel containing 1 g/L SDS. After electrophoresis, the proteins were transferred to polyvinylidene difluoride membranes (Hybond-P; Amersham Life Science) by the Multiblot Electrophoresis Transfer Unit 2051 (LKB). The transfer buffer contained 25 mmol/L Tris, 192 mmol/L glycine, 200 mL/L methanol, and 0.375 g/L SDS. The blots were blocked with 50 g/L powdered nonfat milk in phosphate-buffered saline containing 1 mL/L Tween 20 for 1 h at room temperature, washed, and then incubated for 1 h with a 2000-fold dilution of primary antibody (rabbit anti-PSA, cat. no. A0562; rabbit anti-ACT, cat. no. A022; Dako). Bands were visualized with horseradish peroxidase conjugated to anti-mouse IgG (diluted 3000-fold; Amersham) and a chemiluminescence reaction according to the instructions of the manufacturer (ECL-Plus system; Amersham). The Perfect Protein Western Blot Kit (Calbiochem-Novabiochem) consisting of seven recombinant proteins was used as the molecular marker set.

**Other determinations.** Protein concentrations in tissue extracts were measured with Coomassie Brilliant Blue assay reagent, using bovine serum albumin as the calibrator (13). DNA was assayed using the fluorescence dye Hoechst 33258 in phosphate-buffered saline solution (14).

**STATISTICAL ANALYSIS**

Data were analyzed with the statistical software SPSS 8.0 for Windows (SPSS) and GraphPad Prism 3.00 for Windows (GraphPad Software). The Kruskal–Wallis nonparametric ANOVA with Dunn’s post test, the Mann–Whitney U-test, the Wilcoxon test for paired data, and the calculation of rank correlation coefficients according to Spearman (rs) were performed. Regression analysis for method evaluation was performed using the software EVAPAK 3.01 for Windows according to Passing and Bablok (15). P ≤0.05 was considered statistically significant.

**Results**

**tPSA, fPSA, cPSA, and ACT-PSA in tissue samples.** When the PSA and protein concentrations measured in the separate supernatants after a fourfold extraction as described were summed up and considered as 100%, three extractions produced a mean recovery rate of 97.5% ± 4.84% for tPSA and 96.6% ± 1.2% for protein in 11 different extraction experiments. Thus, a three-step extraction procedure was used for all subsequent experiments. Tissue PSA values were related to the tissue protein, tissue DNA, and wet tissue weight. Only the PSA values related to the tissue protein (μg PSA/mg protein) were used for further presentations because PSA values related to the tissue protein were strongly correlated with PSA values related to the wet weight of the tissue (for tPSA, rs = 0.977; n = 70; P <0.0001; for fPSA, rs = 0.979; n = 70; P <0.0001) or with PSA values per DNA (for tPSA, rs = 0.959; n = 30; P <0.0001; for fPSA, rs = 0.959; n = 30; P <0.0001).

The scatter plots and medians of the tPSA, fPSA, ACT-PSA, and cPSA values in the various tissue samples are shown in Fig. 1. These data and respective comparisons can be summarized as follows:

- fPSA was the major form of PSA in prostatic tissue, independent of the source of the tissue. ACT-PSA yielded only a negligible amount of <0.5% of the tPSA. The minor occurrence of ACT-PSA was verified in comparative measurements by two different ACT-PSA assays based on different anti-PSA antibodies and by the low values of cPSA. The cPSA values were ~3- to 14-fold higher than ACT-PSA but did not exceed 2% of the total PSA.
- The PSA values were significantly correlated with tPSA (rs = 0.964–0.964; P <0.01) and with ACT-PSA (rs = 0.454–0.648; P <0.05) in all tissue samples.
- Total and free PSA were partly different in the
various sources of the prostatic tissue and showed large ranges. The samples obtained from cystoprostectomy patients and histologically confirmed as nondiseased had the lowest values, and the samples from adenomectomy patients the highest values.

- tPSA and fPSA were significantly lower in tissue material obtained from transurethral resection of the prostate than in tissue from adenomectomies, although a similar pattern might be expected. PSA probably is damaged in tissue specimens by heat when the cautering loop is used for resection of the prostate.
- tPSA and fPSA were lower in cancerous than in noncancerous parts of prostate glands from patients with PCa. These differences were not observed for ACT-PSA and cPSA. No significant correlations were found between tumor stage and the tissue concentrations of tPSA, fPSA, and ACT-PSA ($r_s = 0.054, 0.108,$ and $0.225,$ respectively; $P >0.05$) and also between tumor grade and tPSA, fPSA, and ACT-PSA ($r_s = -0.13, -0.168,$ and $-0.310,$ respectively; $P >0.05$).
- The sum of fPSA plus ACT-PSA or cPSA was $\sim 90\%$ of the tPSA, not varying significantly between the different sources of prostatic tissues (ANOVA; $P >0.05$; means, $84.5–92.9\%$). To further elucidate this phenomenon of incomplete recovery, comparative measurements of total and free PSA were performed with two additional assay systems (Abbott AxSYM and DPC IMMULITE). The fPSA/tPSA ratios obtained with the test systems (Roche, $85.4 \pm 12.1$; Abbott, $97.8 \pm 8.1$; DPC, $81.9 \pm 6.6$) differed significantly (ANOVA; $P <0.05$).

PSA ELECTROPHORESIS PATTERN OF PROSTATIC TISSUE

Fig. 2A shows the PSA patterns representative of healthy prostatic tissue (lane 5) and tissue obtained from PCa (lanes 6 and 7) compared with patterns observed in seminal plasma (lane 2), purified PSA (lane 3), and serum from a patient with advanced PCa (lane 4). The immunoassay detected PSA in the serum at $\sim 30$ kDa and $\sim 90$ kDa, which corresponded to fPSA and the ACT-PSA complex, respectively. The PSA bands detected at $>150$ kDa are characteristic of PSA-$\alpha_2$-macroglobulin complexes (16). These complexes were not found in prostatic tissue samples, although ACT was present in prostatic tissue from cancerous and noncancerous sources (Fig. 2B). However, distinct PSA bands below 30 kDa (lanes 5–7) also occurred in all prostatic tissue samples and in seminal plasma. These bands represent internally cleaved PSA molecules (17–19).

PSA GEL FILTRATION PATTERN OF PROSTATIC TISSUE

Gel filtration on Sephacryl S-200 revealed typical PSA profiles for the various prostatic tissue samples studied in comparison with serum, seminal plasma, and purified...
PSA and tissue tPSA concentrations in controls and patients with BPH and PCa \( (r_S = -0.091, 0.307, \text{and 0.241}; P >0.10) \). In addition, the \( \text{fPSA}/tPSA \) and \( \text{ACT-PSA}/tPSA \) ratios in sera did not correlate with the tissue PSA concentrations \( (r_S \text{ between 0.05 and 0.340}; P >0.10) \).

**Discussion**

The different occurrences of free and complexed PSA forms in the serum of PCa and BPH patients and the use of the \( \text{fPSA}/tPSA \) ratio as a promising discriminatory tool between both groups of patients were briefly outlined earlier in the text. A better understanding of why this decreased ratio is typical of PCa patients might be helpful for physicians when interpreting the \( \text{fPSA}/tPSA \) ratio in clinical practice. The results of the present study give further insight into both the biochemical and clinical significance of the molecular forms of PSA.

It has been postulated that PSA is more extensively complexed in PCa cells than in nondiseased prostatic or BPH cells \( (7) \). Consequently, the lower \( \text{fPSA}/tPSA \) ratio in the serum of PCa patients has been assumed to reflect these cellular peculiarities after PSA is released into the blood stream \( (7) \). However, our data for the multiple PSA isoforms in various specimens of prostatic tissue and serum of the same patients (Fig. 1 and Table 1) clearly contradict that hypothesis.

The major form of prostatic tissue PSA is \( \text{fPSA} \), whereas \( \text{ACT-PSA} \) or \( \text{cPSA} \) are <2% of \( \text{tPSA} \). The tissue \( \text{cPSA} \) concentration is 3- to 14-fold higher than that of \( \text{ACT-PSA} \). We believe that these differences are caused by additional PSA complexes that occur in prostatic tissue rather than by a slight cross-reaction of \( \text{fPSA} \) in the \( \text{cPSA} \) assay \( (10) \). For example, prostatic tissue contains high concentrations of \( \alpha_1 \)-antitrypsin \( (20) \), which can form a complex with PSA \( (21) \). Thus, although \( \text{ACT-PSA} \) or \( \text{cPSA} \) contributes <2% of the total tissue PSA, the main proportion of the \( \text{tPSA} \) in serum is bound to \( \text{ACT} \) (Table 1) or measured as \( \text{cPSA} \) \( (10) \). In addition, no correlations were found between tissue and serum PSA isoforms patterns. These quantitative data were corroborated by chromatographic and electrophoretic analyses of PSA and \( \text{ACT} \) in tissue extracts. Although the \( \text{tPSA} \) and \( \text{fPSA} \) were lower in cancerous than in noncancerous parts of the prostate (Fig. 1), no changed pattern of tissue PSA isoforms was observed (Figs. 2 and 3). Moreover, the immunoblots (Fig. 2B) and the immunostaining data by Igawa et al. \( (22) \) did not confirm a higher expression of \( \text{ACT} \) in malignant than in benign prostatic tissue, as described by Björk et al. \( (7) \). These data make it unlikely that the isoform pattern of the serum PSA is a simple reflection of the tissue PSA pattern. Other molecular mechanisms such as the changed proportions of enzymatically active and inactive PSA or posttranslational modification by glycosylation should be considered as possible explanations of the different \( \text{fPSA}/\text{tPSA} \) ratio in the serum of BPH and PCa patients \( (9, 23) \).

Enzymatically inactive PSA, also called “nicked PSA”, is formed by internal proteolytic cleavage and is unable to bind \( \text{ACT} \) and other protease inhibitors \( (23) \). This nicking
process for PSA probably takes place in the extracellular space before PSA reaches the circulation (6). It is assumed that PSA is subjected to this process in healthy and BPH tissue for longer periods of time than in PCa tissue, which additionally secretes PSA directly into the bloodstream because of the altered tissue architecture (6). However, nicked PSA forms have also been found in BPH nodule fluid (8). These PSA forms also occurred in the tissue extracts from both PCa and BPH tissue (Fig. 2). Whatever the reason, PCa serum shows a lower proportion of the cleaved forms than BPH serum (19). This phenomenon could be of great diagnostic significance (19).

The tissue PSA concentrations measured in our study were in the same range as reported by others but somewhat higher (24, 25). These differences could be explained by the use of different PSA assays. Our comparative experiments with various PSA assays support the view that the assays are not completely interchangeable, although all assays were exclusively calibrated against the Stanford 90:10 PSA Calibrator (26). The differences may be related to calibration problems or to the different immunoreactivities of the antibodies used in the assays for detecting free and total PSA (27). In addition, the different fPSA/tPSA ratios obtained with the three assay
systems suggest that the differences of ~10% between the sum of fPSA plus ACT-PSA or cPSA and tPSA may be a result of incorrect calibration of the assays, e.g., for fPSA, rather than incomplete recovery of the PSA isoforms.

There are several reports on PSA expression in BPH and PCa tissue specimens based on immunohistochemistry (22, 28–32), whereas only a few studies determined tPSA with immunoassays (24, 25, 33). The present study thus is the first to date to analyze in detail different sources of prostatic tissue for the molecular PSA forms. Immunohistochemical studies generally indicated a decreased PSA immunoreactivity in PCa tissue compared with benign prostatic tissue. In addition, a dedifferentiation of PCa was found to be associated with a decrease in PSA staining (28, 31). These findings are only partly consistent with quantitative PSA values determined by ELISA techniques in corresponding tissue extracts (24, 33, 34). For example, Pretlow et al. (24) found a decreased PSA content in tumor tissue but did not find relationships between tissue PSA content and the cell differentiation, as Stege et al. (33) did. Our data also showed significant differences between the PSA contents in cancerous and noncancerous parts of the prostate, but no association of tissue PSA concentration with the tumor grade was observed. For a long time, Stege et al. (33) and Pousette et al. (34) recommended tissue PSA as good predictor of the outcome of PCa. However, a recent study showing even higher concentrations of PSA in malignant tissue and no significant differences of tissue PSA in well, moderately, and poorly differentiated PCa tissue challenges these data (25). The reasons for these differences observed between PSA histochemistry and ELISA measurements are not known (24), but it may be easier to relate PSA staining to tumor differentiation when using immunohistochemistry than when measuring PSA in extracts from macroscopic tissue samples. In addition to these contradictory data, the quite variable and overlapping PSA values presumably caused by PSA heterogeneity in malignant prostatic tissue makes it difficult to use tissue PSA as diagnostic marker.

In summary, the amounts of tPSA and the isoforms fPSA, ACT-PSA, and cPSA in prostatic tissue specimens explains neither the concentrations of these analytes in serum nor the characteristics of the fPSA/tPSA ratio in patients with BPH and PCa. In addition, the determination of these analytes in prostatic tissue does not seem to possess diagnostic significance.

This work was supported by grants from the Deutsche Forschungsgemeinschaft (Ju 365/2-1). We are grateful to Bayer Diagnostics, Tarrytown, NY, and Roche Diagnostics, Mannheim, Germany, for providing PSA test kits free of charge. We thank Ines Baumert, Sabine Becker, Silke Klotzek, Katrin Krüger, and Silvia Wagenknecht for valuable technical assistance.

Table 1. Concentrations of tPSA, fPSA, ACT-PSA, and the fPSA/tPSA and fPSA/cPSA ratios in sera of controls and patients with BPH and PCa.

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 10)</th>
<th>BPH (n = 20)</th>
<th>PCa (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>tPSA, µg/L</td>
<td>1.47±0.6 (0.64–3.35)</td>
<td>4.52±1.07 (0.74–40.6)</td>
<td>4.86±0.47 (0.47–21.9)</td>
</tr>
<tr>
<td>fPSA, µg/L</td>
<td>0.20±0.1 (0.10–0.47)</td>
<td>1.00±0.18 (0.22–27.7)</td>
<td>0.60±0.04 (0.32–22.2)</td>
</tr>
<tr>
<td>ACT-PSA, µg/L</td>
<td>1.09±0.48 (0.48–3.21)</td>
<td>3.28±0.44 (24.3)</td>
<td>4.34±0.4 (21.0)</td>
</tr>
<tr>
<td>fPSA/tPSA, %</td>
<td>22.8% (11.8–36.7)</td>
<td>24.1% (14.8–55.9)</td>
<td>11.7% (2.1–32.0)</td>
</tr>
<tr>
<td>ACT-PSA/tPSA, %</td>
<td>73.9% (60.8–95.8)</td>
<td>73.4% (35.6–119)</td>
<td>85.5% (59.3–102)</td>
</tr>
</tbody>
</table>

*Data are given as medians (ranges). Patients with cystoprostatectomy and confirmed non-prostatic disease were considered controls without prostatic disease. Patients with open adenomectomy and transurethral resection of the prostate were combined with the BPH patients (for further details, see Materials and Methods). All PSA concentrations were measured with Roche tests.

References


