also created specific reference ranges for free and bound PSA. In the same study the authors have not shown any correlation between the age of the patient and the ratios free/total, bound/total and free/bound PSA. In spite of the fact that the serum level of each molecular form elevates with increasing age by 3% per year, this age dependence is not observed when we divide the level of one form by the level of another form, thus creating a ratio.

In some studies the authors show the existence of dependence, or even direct proportionality between the f/t PSA ratio and PSA. Men with higher PSA levels have lower values of the f/t PSA ratio. It is obvious that patients with lower PSA values should have an optimal cut-off value of the PSA f/t ratio higher than patients with higher PSA values. To prove this hypothesis and enable creation of a series of cutpoints for different serum PSA concentrations, further studies are needed (Partin et al., 1996; Abrahamson et al., 1997; Lukeš et al., 1998).

Data about the relation of the free PSA level and prostate volume are controversial in the literature. Partin et al. (1996) describe the influence of the prostate volume on the f/t PSA ratio; they state that with increasing prostate volume the values of the f/t PSA ratio also increase. On the contrary, Yemoto et al. (1996) have not found any correlation between the prostate volume and absolute fPSA concentration or f/t PSA ratio.

Elgamal et al. (1996) have demonstrated that the fraction of free PSA correlates well with the prostate volume ($r = 0.49$, $P = 0.005$) and Gleason score ($r = 0.37$, $P = 0.036$). The correlation with favorable histology was also supported by other authors (Carter et al., 1997). Catalona et al. (1998) have shown significant elevation of the probability of favorable pathology (Gleason score < 7, tumor volume < 10% of prostate volume and its limitation to the organ – T1, T2, without detection of metastases in lymph nodes) with increasing proportion of free PSA ($P < 0.001$).

Determination of the f/t PSA ratio increases the specificity of PSA examination after PC detection and at the same time enables elimination of a number of unnecessary prostate biopsies in patients with negative rectal examination and PSA values in the range 4–10 ng/ml.

The future of PSA

Olsson et al. (1997) introduced into clinical practice the reverse transcriptase polymerase chain reaction (RT-PCR) test for detection of PSA positive cells from peripheral blood. He states that the accuracy of the staging performed by using serum PSA concentrations and RT-PCR for PSA positive cells in peripheral blood increased to 93%.

When the pre-operation value of serum PSA was higher than 10 ng/ml and RT-PCR for PSA-positive cells in peripheral blood was negative, 81% of the patients who underwent radical prostatectomy had PC actually limited only to the gland itself. On the contrary, when the PSA level of the patients was higher than 10 ng/ml and the RT-PCR test was positive, 90% of the patients had positive boundary or invasion into seminal vesicles, or their lymph nodes were affected. In case that perineural invasion of PC was detected by prostate biopsy and RT-PCR was positive, the authors have found extraprostatic invasion of PC in the radical prostatectomy specimen in 100% of cases (Olsson et al., 1997). Similar results were presented by Rubin et al. (1997). Gao et al. (1999), on the contrary, have not supported these results.

Conclusion

When PSA was introduced clinically in 1986 the impact that this tumor marker would have on detecting, staging and monitoring prostate cancer was not fully understood, and it can only be fully appreciated in retrospect. During the last decade our understanding of the molecular structure, function and clinical usefulness of PSA has greatly advanced. Many investigators have made significant contributions to improving the sensitivity and specificity to detect early, curable prostate cancer and, despite its present limitations, PSA remains the most useful tumor marker in oncology today.

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