Clinical Application of Ultrasensitive Prostate-Specific Antigen Assays

Junker et al. (1) measured prostate-specific antigen (PSA) levels in sera of subjects who underwent cystoprostatectomy for bladder cancer. Their aim was to establish baseline levels of PSA following prostate removal in patients who do not have prostate cancer. They calculated the “biological lower detection limit,” defined as PSA concentration detected in PSA-free human serum plus 3 standard deviations (SDs). This value was 0.29-0.63 ng/mL, and they concluded that ultrasensitive PSA assays have negligible advantages in monitoring patients with prostatic carcinoma. This conclusion is erroneous and is not supported by many other reports in the literature that were not cited by Junker et al.

1) Ultrasensitive PSA assays with detection limits of 0.01-0.001 ng/mL (2-4) allow accurate measurement of PSA levels at very low concentrations.

2) The term “biological detection limit” (5) is used inappropriately, since the definition of Junker et al. matches a residual cancer detection limit (RCDL).

3) Prestigiacomo and Stamey (4) and Stamey (6) calculated RCDL to be 0.05-0.07 ng/mL. The values quoted by Junker et al. are fourfold to sixfold higher.

4) After radical prostatectomy, 60%-80% of patients have PSA levels lower than 0.01 ng/mL and as many as 20% have PSA levels lower than 0.001 ng/mL (2,3,7). The merits of ultrasensitive monitoring have been clearly documented (4,7). Changes in PSA levels between 0.001 and 0.1 ng/mL are clinically important (8).

5) Junker et al. attempted to explain their results by speculating that there may be cross-reacting substances, including kallikreins, in serum. These proposals are not correct, since the PSA levels are lower than 0.01 ng/mL in the majority of serum samples from females and prostatectomized males (3,7-9). Junker et al. claim that PSA may be produced by peripheral blood cells and other tissues. The cited papers did not demonstrate PSA protein production by such cells but describe the presence of traces of PSA messenger RNA, detected by polymerase chain reaction (10,11). The literature on nonprostatic PSA (12) does not support the contribution of other tissues to serum PSA. Junker et al. mention the periurethral glands as possible contributors to serum PSA, but Oesterling et al. (13) concluded that the periurethral glands do not significantly influence serum PSA levels.

Why did Junker et al. calculate much higher RCDLs? Cystoprostatectomies in France may be performed differently from those in the United States, which would result in residual prostatic tissue. More likely, the discrepancies originated from the inability of the methods used to discriminate accurately PSA levels below 0.05 ng/mL. The imprecision at such PSA levels will result in high SDs, and the RCDL will be unrealistically high when the mean is added to 3 SDs. RCDL becomes lower as the methods used for PSA become more sensitive (4).

Ultrasensitive PSA assays with biological detection limits of 0.01 ng/mL or lower detect relapse at least 1 year earlier than assays with biological detection limits around 0.1 ng/mL (4,7,8). Recently, it has been shown that initiation of early radiotherapy due to isolated elevation of serum PSA levels following radical prostatectomy significantly improves patient outcomes (14).

References


8) Yu H, Diamandis EP, Wong PY, Nam R, Trachtenberg J. Detection of prostate cancer relapse with prostate specific antigen monitoring at levels between 0.001 to 0.1 μg/L. J Urol 1997;157:913-8.


Notes

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