

The Cutoff Level of Free/Total Prostate Specific Antigen (f/t PSA) Ratios in the Diagnosis of Prostate Cancer: Current Status and Future Perspectives

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Editorial

PSA is one of the most important biomarkers for detecting prostate cancer and guiding decisions to biopsies of the prostate. Despite its adequate sensitivity, the use of PSA testing is limited by a significant lack of specificity, which can result in unnecessary biopsies. Recent findings emphasize the limitation of these PSA threshold values to discriminate between prostate cancer and benign disease in asymptomatic men [1-3]. Therefore clinicians tried to improve a new diagnostic biomarker for clinically significant PCa. One of the most promising marker is PSA derivatives such as free PSA and its ratio to total PSA (%f/t PSA).

Murray et al. compared 3 PSA parameters (%f/t PSA, PSA velocity, and PSA density) in 303 men undergoing initial prostate biopsy and found that %f/t PSA was superior than other PSA parameters with a sensitivity and specificity of 70.8%, and 67.4%, respectively [4].

Use of the f/t PSA ratio has been shown to improve specificity in detection of prostate cancer. No definitive data are available indicating the optimal %f/tPSA that should be applied. Despite the various cutoff levels in the literature, a low%f/t PSA is strongly associated with unfavorable tumor characteristics. Recently published data demonstrated that the cumulative probabilities of Pca detection at 3 years were 64.5, 41.2, 28.5, and 14.3 % for patients with f/t PSA ratio ≤ 0.08 , 0.09–0.13, 0.14–0.22, and ≥ 0.23 , respectively [5]. This was a retrospective study and had several limitations such as biases for time from populations screening to diagnosis. However they showed that f/t PSA ratio was a strong predictor of future cancer detection. Partin et al. suggested using f/t PSA ratio 15%, which would detect all advanced, non-organ confined, and large volume tumors, while avoiding 80% of biopsies in men with insignificant disease, particularly in the intermediate range of total PSA (4.1-10 % ng/mL) [6]. Catalona et al. suggested a cutoff of 24% to detect 90% of cancers and to avoid 18% of benign biopsy findings in patients with a PSA value 2.6-4.0 ng/mL [7]. In an update, Catalona et al. examined a variety of cutoffs, some of which were as low as 10%. Other investigators have recommended cutoffs of 18-27% [8]. Although the cutoff value of f/t PSA ratio is conflicting, in our previous study, 10% cutoff had a sensitivity of 37.6% and specificity of 95% in all age groups [9].

In addition, age-specific reference rates have been proposed as a means of improving specificity and positive predictive value of the total PSA in screening for prostate cancer. Previous studies demonstrated that the total PSA level is significantly related to age; however, an age-specific f/t PSA ratio has not yet been determined. Chun et al. [10] and our previous study hypothesized that a relationship between f/tPSA ratio and age can be established [9]. Age-specific cutoffs were also reported by Catalona et al. as 20%, 26%, and 28% f/t PSA ratios for ages 50-59 years, 60-69 years, and 70-75 years, respectively [8].

In our previous study, the f/t% PSA cutoff points were determined to be 10%, 15%, 15% and 10% in 50-59years, 60-69years, >70 years, and all ages categories in patients with initial PSA level of 4-10 ng/ml, respectively [9]. It was accepted that free %PSA was not effective in the PSA range of 10-20 ng/ml. But in a Chinese multicenter study the authors claimed that %f/t PSA over 23.4% may delay or avoid unnecessary biopsy in patients with PSA 10-20 ng/ml, aged ≥ 60 years old. However they also emphasized the lower chance of PC a detection in Chinese compared with the Western population at the same PSA level [11].

Thus, the %f/t PSA is increasingly used and can reduce the number of unnecessary biopsies, but in the perspective of future, usage of %f/t PSA with new biochemical markers such as Prostate

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Specific Membran Antigene (PSMA) may be increased the value of PSA and its derivatives in the diagnosis of significant PCa. Patients with very low PSA values can refer to PSMA-ligand PET/CT imaging in alternative imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI).

In addition, magnetic resonance imaging (MRI) which is a functional technique that gives physiologic information on anatomic structures and malignant lesions, is currently the best imaging method for PCa detection. However MRI does not rule out prostate biopsy alone and it does not provide PSA significance.

The choice of the best cutoff for the f/t PSA ratio depends on a variety of arguments that mainly include the combination of screening modalities used. The age related changes warrant further investigations in a larger, multicentric and multinational population to improve the clinical use of f/t PSA cutoffs.

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