

FREE/TOTAL PSA RATIO IDENTIFIES MEN WHO HAVE LOWER
PROBABILITIES OF HAVING A CONCURRENT POSITIVE PROSTATE
BIOPSY

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Aim: To identify a subset of men with elevated total prostatic-specific antigen (PSA), particularly in the range of 4.0-20 ng/ml, who are at low risk of having adenocarcinoma in a concurrent prostate biopsy.

Material and Methods: The patient sample consisted of 296 men without previous history of prostate cancer, ranging in age from 36 to 85 years (mean=67.8 years), and having a total serum PSA between 4-20 ng/ml. All patients had a prostate biopsy interpreted at our institution as either "positive" (adenocarcinoma present) or "negative" (no detectable cancer, high grade prostatic intraepithelial neoplasia or "suspicious" glands). Biopsies were taken during or soon after (mean = 25 days) sera collection date. External reference standards (Stanford University) for both free (DPC-Immulin) and total (TOSOH) PSA assays used in an equimolar mixture of 90% PSA: α -1 antichymotrypsin complex and 10% free-PSA to re-calibrate the two assays. A "corrected" free/total (f/t) PSA ratio was calculated and a f/t ratio cutoff of $\geq 15\%$ was chosen to identify patients with low probabilities of having a positive biopsy. All results were analyzed using standard parametric methods and non-parametric logistic regression analysis.

Results: The ability of f/t PSA ratio to discriminate *negative* from *positive* prostate cancer was very significant ($p < 0.0001$). For patients with a total PSA value of < 10 ng/ml, at a f/t ratio cut-off of $\geq 15\%$, 79/96 (82.3%) did not have positive biopsies. In a small subset of patients with a total PSA value of 10-20 ng/ml, at the same f/t ratio cut-off, 7/8 (87.5%) did not have a *positive* biopsy. Applying logistic regression analysis to the entire patient sample (N=296) to predict the diagnostic outcome, the f/t ratio yielded a receiver operator curve with an area under the curve (AUC) of 0.653 versus total PSA which had a AUC=0.548 ($p < 0.0001$). The overall negative predictive value for this model was 77.6%.

Conclusion: In a subset of patients (N=104) with a f/t PSA ratio of $\geq 15\%$, the test correctly predicted a negative biopsy result in 82.3%. The *positive* biopsy rate (17/104) in this subset is more than that expected for men with normal total PSA values of < 4.0 ng/ml, but less than that expected for men with PSA between 4-10ng/ml.