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Editorial comment for “Association between Glomerular Filtration Rate and Free, Total, and Percent Free Prostate Specific Antigen” (#URL-D-09-00510R1) for UROLOGY

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Chronic kidney disease (CKD) is common. According to several analyses of the National Health and Nutrition Examination Surveys (NHANES), as much as 13% of the non-institutionalized US adult population belongs to CKD stages 1 to 4. This includes 3.2% with stage 2 (GFR 60–89 mL/min/1.73m²) and 7.7% with stage 3 (GFR 30–59 mL/min/1.73 m²) (1). This high prevalence of renal impairment affects the analysis of blood biomarkers that are cleared by renal elimination.

The low molecular mass of free PSA (fPSA) is compatible with clearance by glomerular filtration; this has been confirmed in several investigations. The half-life of fPSA after successful renal transplantation is 17 h, similar to that of creatinine (23 h) (2). Patients with terminal renal failure show significantly increased levels of fPSA and %fPSA (3,4). Percent fPSA was 39.5% in hemodialysis patients and 39.6% in patients on continuous ambulatory peritoneal dialysis, compared to 28.1% in controls (4). Among 101 patients with moderate renal failure with median GFR of 23 mL/min/1.73m² (range 8–83 mL/min/1.73m²), Bruun et al showed a significantly higher level and percentage of fPSA, 0.45 µg/L and 47.2%, respectively, compared to controls, 0.29 µg/L and 29.9%, respectively (5). The strength of their study was the use of iothexol clearance, a gold standard for measurement of GFR.

The current paper {URL-D-09-00510} takes another approach. The authors used a large group (n=3782) from NHANES, which is a well-established cohort with a representative population. The participation rate was high. The authors used estimated GFR (eGFR) from the 6-variable MDRD formula; this approach is less accurate than iothexol clearance but was the only possible way to define GFR in this large cohort. Among 382 men with eGFR 15–59 mL/min/1.73m², fPSA and %fPSA were significantly elevated, and values were also higher in those with eGFR 60–89 mL/min/1.73m². The strength of this study is the large sample size that ensures representative material.

Conflict of Interest Statement: Dr. Hans Lilja holds patents for free PSA and hK2 assays.

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Both the current report, and a recently published study by Bruun et al, shows that fPSA and percent fPSA are importantly influenced by moderately impaired renal function in men with chronic kidney disease. Interestingly, both demonstrate that fPSA is also affected by slight renal impairment (GFR 60–89 mL/min/1.73m²). As noted above, slight and moderate renal impairment are highly prevalent in the general population, and they are even more frequent among elderly men. This means that a significant number of men may have reduced elimination of fPSA, which has implications for the use of %fPSA to discriminate prostate cancer from benign prostate hyperplasia. Use of the current clinical decision limits for percent fPSA could cause some men with decreased GFR and prostate cancer to be misdiagnosed as having benign disease. Therefore, one alternative could be to not use fPSA to diagnose prostate cancer in these patients.

This new knowledge also does, however, create the possibility for strengthening %fPSA in the diagnosis of prostate cancer, especially for screening purposes. The present clinical decision limits were developed without this knowledge. Contingent of a proper accounting for the GFR, %fPSA may therefore have an even greater potential for differentiating prostate cancer from benign prostate hyperplasia.

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