Assessment of Prostate Cancer Risk in Men with PSA < 1.5

Whitney N. Stanton, E. David Crawford, *MD*, Paul Arangua, John Hoenemeyer, *MD*,
Francisco G. La Rosa, *MD*, Adrie van Bokhoven, *PhD*, M. Scott Lucia, *MD*,
Wendy Poage[1], Gretchen Hoyer, and Priya N. Werahera, *PhD*

University of Colorado Anschutz Medical Campus, Aurora, CO; [1]Prostate Condition Education Council,
Aurora, CO

Email for contact author: whitney.stanton@colorado.edu

Introduction and Objective: Prostate Specific Antigen (PSA) screening remains controversial primarily because of over detection and over treatment. There is an unmet clinical need to identify patients at increased risk for high-grade (HG – Gleason Score ≥7) prostate cancer (PCa) since PSA has low sensitivity. Combining PSA with well-validated prostate cancer biomarkers (PCM) can improve risk assessment. We investigated the performance of three PCMs (phi – prostate health index, 4KScore, and SelectMDx) on patients with PSA levels < 1.5 ng/mL that represent a "safe zone" where risk of any PCa is <0.5% in 5 years and HG PCa is rare.

Methods: In 2012, 2015, and 2016, 652 men were screened for prostate cancer during the annual Prostate Cancer Awareness Week in September at the University of Colorado Hospital. This study was supported by Prostate Condition Education Council and the Schramm Foundation. phi is evaluated using p2PSA, total PSA (tPSA), free PSA (fPSA) in serum. Phi < 27 suggests absence of PCa. 4KScore is a blood test that incorporates a panel of four kallikrein protein biomarkers: tPSA, fPSA, intact PSA, human kallikrein protein, and clinical information. A 4KScore < 7.5% suggest absence of HG PCa. The SelectMDx post-DRE urine test measures the mRNA levels of the homeobox C6 and distal-less homeobox 1 biomarkers. SelectMDx score of 0% indicates absence of HG PCa.

Results: No patients with a PSA < 1.5 had SelectMDx > 0% whereas 43.2% of men had phi ≥ 27 and 17.5% men had 4KScore ≥ 7.5% (Table). For patients with PSA between 1.5-3.99, 2% (2/83), 69.6% (94/135), and 36.8% (21/57) had positive SelectMDx, Phi, and 4KScore, respectively. If we selected Phi < 52.7 and 4KScore < 20% as cutoffs to indicate absence of HG PCa based on published literature then only one patient in this cohort with a PSA < 1.5 would be at risk for HG PCa with a 4KScore ≥ 20.

Table: Test Results of PCMs for Patients with PSA < 1.5 ng/mL

Year	PCM Performed	Number of Patients	Median Age (range)	Abnormal Test Results (%)
2012	Phi	67	64 (41-86)	29/67 (43.2%)
2015	4KScore	80	68 (47-89)	14/80 (17.5%)
2016	SelectMDx	80	68 (41-100)	0/80 (0%)

Conclusions: Men with PSA <1.5 ng/mL are at very low risk for HG PCa. This PSA range may represent a "safe zone." An adjustment in cut-off levels is necessary with both phi and 4KScore since it is desirous PCMs have an undetectable or very low rate of positivity in this low PSA range. Men with PSA between 1.5-3.99 with positive PCM results may be referred for further evaluation.