Poster No. O313

HIV Glasgow Drug Therapy 2014

Predictive value of Prostate Specific Antigen (PSA) for prostate cancer (PCa): A nested case control study in EuroSIDA

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BACKGROUND

- PSA>4 µg/L is often used to identify men at high risk for prostate cancer to undergo further screening.
- Previous studies have identified lower PSA levels in HIV+ compared to HIV- men[1], which may lead to higher false negative rates than in HIV- men.
- The appropriateness of PSA>4 µg/L as a clinical indicator for high PCa risk in HIV+ men is not well defined.

AIM

To describe the kinetics and predictive value of PSA and other associated biomarkers of prostate cancer risk in HIV+ men.

METHODS

Design

Men with PCa(n=21) and up to 2 matched controls(n=40) with prospectively stored plasma samples before PCa (or matched date in controls) were selected. Cases and controls were matched on date of first and last sample, age, region of residence, and CD4 count at first sample date.

Measurements

Total PSA(tPSA), free PSA(fPSA), testosterone and sex hormone binding globulin(SHBG) were measured on serial plasma samples.

Statistical methods

Conditional logistic regression models investigated associations between markers and PCa. Sensitivity and specificity of using tPSA >4 µg/L to predict PCa was calculated. Mixed models were used to describe kinetics.

RESULTS

Baseline

- 61 men were included with a median 6(IQR 2-9) years follow-up. Time between last sample and PCa was 7 (4-11) months. Baseline characteristics for cases and controls are shown in **table 1**, and were well matched at first sample.

Marker levels and PCa

- Median baseline and latest marker levels together are shown in **figure 1**. Median tPSA and fPSA levels were higher in cases than controls at both baseline and latest sample. SHBG levels were similar in cases and controls at first and last sample.
- Both tPSA and fPSA increased significantly over time in cases (**figure 2**), but were stable in controls. Change in testosterone and SHBG levels over time were similar in cases and controls.
- Higher levels of tPSA and fPSA were associated with higher odds of PCa at both first and last sample. Elevated tPSA values in cases were detectable ≥5 years before PCa(P<0.01). Testosterone and SHBG levels were not associated with PCa at either baseline or latest sample (**figure 3**).

Predictive value of total PSA

- The most informative predictor of PCa was tPSA (AUC=0.9), followed by fPSA(0.8). Testosterone(AUC=0.5) and SHBG(0.5) were poor predictors of PCa.
- tPSA level>4µg/L had 99% specificity and 37% sensitivity. Performance was best in the year prior to PCa (specificity:99%, sensitivity:88%).

CONCLUSIONS

PSA was highly predictive of PCa in HIV+ men. Our results indicate that PSA screening in HIV + men may be useful, and further work is needed to identify potentially age-related cut-offs to maximise sensitivity and specificity to identify those for further evaluation for early stages of PCa.

[1]Marcus JL, Chao CR, Leyden WA, et al. Prostate cancer incidence and prostate-specific antigen testing among HIV-positive and HIV-negative men. *J Acquir Immune Defic Syndr.* 2014;66(5):495-502.

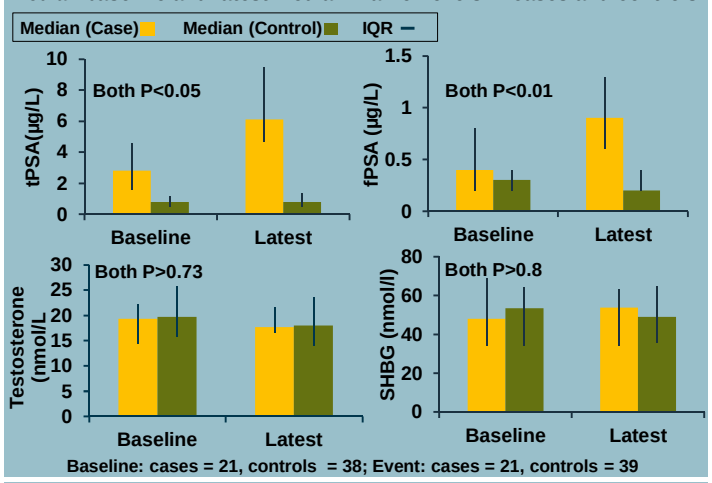
Table 1 **Baseline† characteristics of cases and controls**

Factors	Total	Prostate cancer		P
		Cases	Controls	
		N (%)		
Total	61 (100)	21 (100)	40 (100)	Na
Risk group				
Homosexual	47 (77.0)	17 (81.0)	30 (75.0)	0.98
Heterosexual	7 (11.5)	2 (9.5)	5 (12.5)	
IDU	2 (3.3)	0 (0.0)	2 (5.0)	
Non-white Ethnicity	4 (6.6)	0 (0.0)	4 (10.0)	0.99
prior NADM	59 (96.7)	19 (90.5)	40 (100)	0.99
prior ADM	55 (90.2)	21 (100)	34 (85.0)	0.99
On treatment	58 (95.1)	20 (95.2)	38 (95.0)	1.00
HBV+	4 (6.6)	3 (14.3)	1 (2.5)	0.12
HCV+	1 (1.6)	0 (0.0)	1 (2.5)	1.00
		Median (IQR)		
Age	51 (48,57)	52 (49,57)	51 (47,56)	0.18
CD4 count (cells/mm3)	437 (243,610)	460 (260,610)	426 (230,595)	0.07
log_{10} HIV VL (copies/ml)	1.9 (1.6,2.6)	1.9 (1.6,2.6)	2.0 (1.6,2.6)	0.40

†baseline was date of first plasma sample

Figure 1

Median baseline and latest median marker levels in cases and controls



Baseline: cases = 21, controls = 38; Event: cases = 21, controls = 39

Figure 3

Marker levels by time before diagnosis in cases and controls with superimposed Loess curves

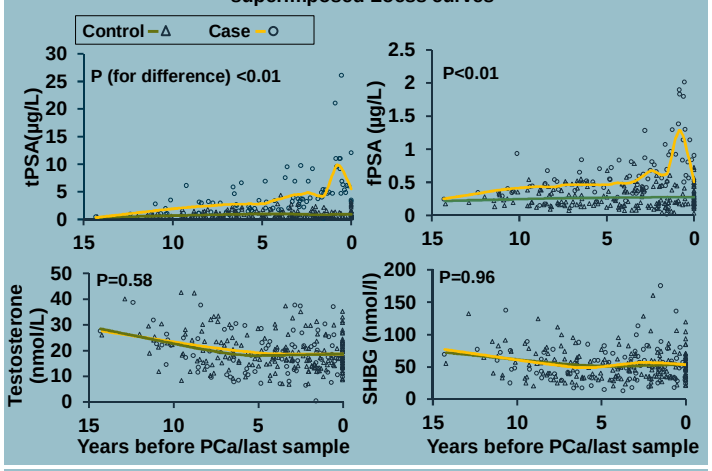
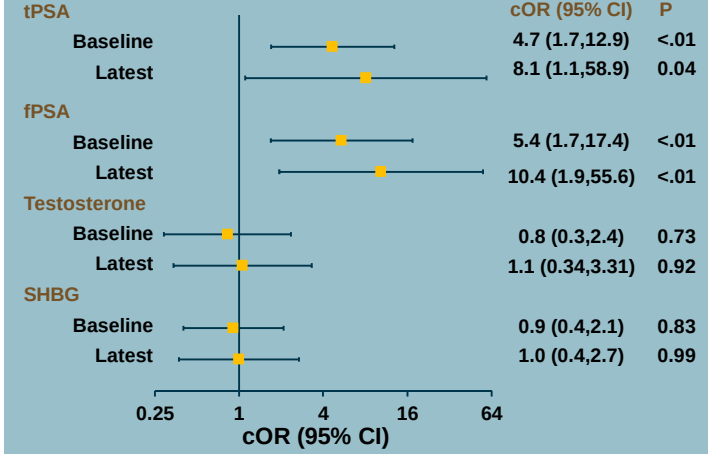


Figure 3

Conditional odds ratios (cOR) of PCa for baseline and latest marker levels



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