PSA Density Kinetics Predict Biopsy Grade Progression on Prostate Cancer Active Surveillance

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Introduction and Objectives:

- PSA density (PSAd) has been associated with risk of progression on AS when measured at diagnosis or confirmatory biopsy, yet no study has examined the correlation between AS outcomes and serial PSAd measurement during follow up
- We investigated the prognostic impact of serial PSAd measurement (PSAd kinetics) in men enrolled in AS to evaluate whether PSAd kinetics independently predict pathologic grade progression on AS biopsy

Methods:

- 1290 men enrolled in AS at the MGH (1997-2016)
- Identified 453 patients with Gleason Grade Group 1 disease and ≥ 2 PSAd at least 1 year apart during AS
- Primary outcome: pathologic grade progression on biopsy
- PSAd kinetics were plotted with LOESS regression and analyzed with Cox model and compared to a multivariable model of predictors at diagnosis (age, NCCN risk, gleason grade, disease volume and PSAd)
- For PSAd kinetics, PSAd was used as continuous time-varying variable, reevaluating the risk of disease progression each time a measurement was available
- An extended Kaplan Meier estimator used to examine the risk of progression stratified by PSAd quartiles

Results:

- Median follow-up for the entire cohort was 5.9 years
- 137 men (30.2%) experienced progression on follow up biopsy at median of 3.3 years post diagnosis with 162 (35.8%) undergoing treatment
- PSAd varied significantly during AS with higher levels observed in patients who progressed (Figure 1)
- After adjusting for covariates, PSAd kinetics had the highest-ranking hazard ratio for biopsy grade progression [2.01, 95% CI: 1.72-2.36, p<0.001]
- Progression risk was strongest for patients with a PSAd value in the fourth quartile of all cohort PSAd values (>0.16 ng/ml^2) with a distinct curve deviation (HR 4.25, 95% CI: 2.49-7.24, p<0.001) (Figure 2)
- Adding either PSAd kinetics or PSAd in quartiles to the reference model significantly improved the c-index of the cox regression (0.75 vs 0.69)

Conclusions:

- PSAd kinetics are a strong independent predictor of pathologic progression on AS
- PSAd values greater than 0.15 ng/ml^2 at any time during AS should alert the treating physician to utilize close scrutiny and consider repeat biopsy
- The components of PSAd are already part of routine AS protocol, so monitoring PSAd over time confers no additional cost or burden to the patient and can be easily integrated into clinical practice to improve risk stratification for men with prostate cancer

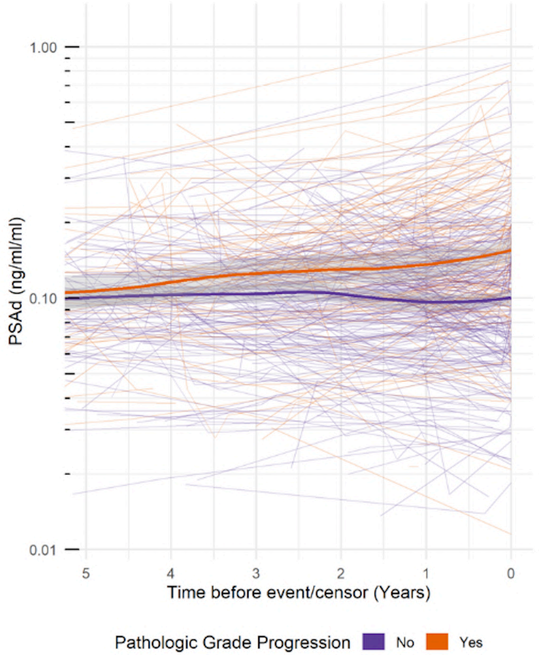

Figure 1: Spaghetti plot of PSAd per year before pathologic grade progression/censor date with logarithmic scale on y-axis. Individual trajectories are plotted in purple for censored patients and orange for disease progression. Smooth trend lines added using locally estimated scatterplot smoothing (LOESS).

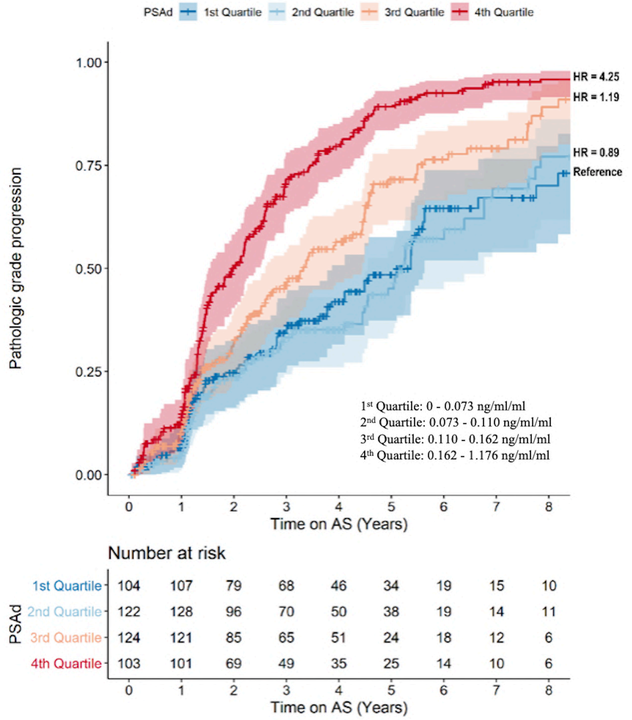

Figure 2: Extended Kaplan-Meier estimates for pathologic grade progression on AS biopsy stratified by PSAd kinetics quartiles. Hazard ratios (HR) per PSAd quartile calculated from Cox model and adjusted for reference characteristics.