**Dietary and Lifestyle Factors and Risk of Progression in Contemporary Active Surveillance Patients**

**Introduction and Objective**: Men diagnosed with prostate cancer frequently change their diet or lifestyle in an effort to decrease their risk of developing aggressive disease. Men managed with active surveillance (AS) may feel a greater need to modify risk factors because their cancer is untreated. We evaluated the influence of diet and lifestyle on risk of prostate cancer biopsy progression in the largest prospective AS cohort in the US.

**Materials and Methods**: Diet and lifestyle questionnaires were completed by AS participants at enrollment. Biopsy progression was defined as Gleason score 7 or higher, or increase in tumor volume at annual surveillance biopsy. We also evaluated progression indicated by upgrading only (Gleason $\geq$7). Analysis focused *a priori* on 38 nutrients/food groups, 9 vitamin supplements, 7 medication variables, and 2 lifestyle variables. Data were analyzed by Cox proportional hazards regression with results expressed as hazard ratio (HR) and 95% confidence interval (CI); dietary variables were adjusted for calories by the residual method.

**Results**: There were 736 men in the analysis, of whom 235 (32%) progressed. Median follow-up was 2.7 years. In multivariable analyses, current cigarette smokers had significantly increased risk of biopsy progression (HR=2.6, p=0.004) (full model in TABLE). When biopsy progression was confined to Gleason upgrading, use of aspirin for 3 or more years prior to diagnosis was associated with a significant 50% decreased risk of upgrading, HR=0.5, p=0.019. Diet variables and supplements were not associated with risk.

**Conclusions**: Cigarette smoking was significantly associated with risk of progression, and long-term use of aspirin prior to diagnosis was associated with decreased risk of upgrading. These associations have not previously been reported for progression of men in AS. Although these associations should be viewed with caution due to the large number of variables tested, their potentially important impact on risk requires validation.

| | **BIOPSY PROGRESSION BY UPGRADING OR TUMOR VOLUME** | | **BIOPSY PROGRESSION BY UPGRADING (Gleason$\geq$7)** | |
|---|---|---|---|---|
| **VARIABLES** | **HR (95% CI)** | **p-value** | **HR (95% CI)** | **p-value** |
| Year of diagnosis (continuous) | 1.24 (1.17, 1.31) | <0.0001 | 1.26 (1.13, 1.42) | <0.0001 |
| Logarithm PSA density (continuous) | 1.62 (1.17, 2.24) | 0.016) | 1.86 (1.20, 2.88) | 0.005 |
| Number of positive biopsy cores (>1 vs. 1) | 1.81 (1.54, 2.12) | <0.0001 | 1.75 (1.10, 2.77) | 0.018 |
| % of biopsy involved with tumor (continuous) | 1.03 (1.02, 1.04) | <0.0001 | 1.05 (1.03, 1.07) | <0.0001 |
| **Current smoker (yes vs. no)** | **2.59 (1.36, 4.92)** | **0.004** | ***[Not in model]*** | **--** |
| **Aspirin use before diagnosis (3+ vs. <3 years)** | ***[Not in model]*** | **--** | **0.54 (0.32, 0.90)** | **0.019** |