Association Between Lead Time and Prostate Cancer Grade:
Evidence of Grade Progression from Long-term Follow-up of Large Population-based Cohorts Not Subject to Prostate-specific Antigen Screening.


BACKGROUND: Lead time (LT) is of key importance in early detection of cancer, but cannot be directly measured. We have previously provided LT estimates for prostate cancer (PCa) using archived blood samples from cohorts followed for many years without screening.

OBJECTIVE: To determine the association between LT and PCa grade at diagnosis to provide an insight into whether grade progresses or is stable over time.

DESIGN, SETTING, AND PARTICIPANTS: The setting was three long-term epidemiologic studies in Sweden including men not subject to prostate-specific antigen (PSA) screening. The cohort included 1041 men with PSA of 3-10 ng/ml at blood draw and subsequently diagnosed with PCa with grade data available.

OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Multivariable logistic regression was used to predict high-grade (Gleason grade group ≥2 or World Health Organization grade 3) versus low-grade PCa at diagnosis in terms of LT, defined as the time between the date of elevated PSA and the date of PCa diagnosis with adjustment for cohort and age.

RESULTS AND LIMITATIONS: The probability that PCa would be high grade at diagnosis increased with LT. Among all men combined, the risk of high-grade disease increased with LT (odds ratio 1.13, 95% confidence interval [CI] 1.10-1.16; p<0.0001), with no evidence of differences in effect by age group or cohort. Higher PSA predicted shorter LT by 0.46 yr (95% CI 0.28-0.64; p<0.0001) per 1 ng/ml increase in PSA. However, there was no interaction between PSA and grade, suggesting that the longer LT for high-grade tumors is not simply related to age. Limitations include the assumption that men with elevated PSA and subsequently diagnosed with PCa would have had biopsy-detectable PCa at the time of PSA elevation.

CONCLUSIONS: Our data support grade progression, whereby following a prostate over time would reveal transitions from benign to low-grade and then high-grade PCa.
PATIENT SUMMARY: Men with a longer lead time between elevated prostate-specific antigen and subsequent prostate cancer diagnosis were more likely to have high-grade cancers at diagnosis.

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