

## Leukocyte Telomere Length and Prognosis of Localized Prostate Cancer

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**BACKGROUND:** Telomeres are the protective structure at the ends of each chromosome and play an important role in maintaining genomic integrity. Interindividual variation of telomere length in peripheral blood leukocytes has been associated with the risks of developing many human diseases including several cancers. The association between leukocyte telomere length (LTL) and prognosis of localized prostate cancer has not been studied.

**HYPOTHESIS:** We hypothesized that LTL would have significant predictive value for risk of biochemical recurrence (BCR) and progression in localized prostate cancer patients.

**METHODS:** We recruited ~1,800 non-Hispanic white men with previously untreated prostate cancer from the University of Texas MD Anderson Cancer Center. Relative LTL was measured by real-time polymerase chain reaction. We compared LTL among patients of different aggressiveness at diagnosis. We also analyzed the association of LTL with prognosis (biochemical recurrence and progression) by estimating hazard ratios (HRs) and 95% confidence intervals (CIs) using a multivariable Cox proportional hazard regression model.

**RESULTS:** The median follow-up time was 44.3 months. The majority of patients were between 55 and 65 years old, overweight or obese, non-smokers or former smokers, had predominantly Gleason Score (GS) of 6 and 7, had D'Amico intermediate-risk disease, and had PSA at diagnosis < 10 ng/ml. About half of the patients received radical prostatectomy. We observed an inverse relationship between LTL and aggressiveness of prostate cancer at diagnosis: patients with higher GS had significantly shorter LTL than those with lower GS ( $P=0.002$ ). Furthermore, shorter LTL was significantly associated with worse prognosis in these patients. In multivariate Cox analysis adjusting for age, BMI, smoking status, and smoking pack-year, when patients were dichotomized into long and short LTL groups based on the median LTL, compared to patients with longer LTL, those with short LTL had significantly increased risks of biochemical recurrence (HR=1.54, 95% CI 1.01 – 2.34). There was a significant dose-response in quartile analysis: compared to patients in the longest LTL quartile, those in the 3rd, 2nd, and shortest quartiles of LTL had HRs of 1.39 (95% CI, 0.72-2.64), 1.79 (95% CI 0.97-3.30), and 1.84 (95% CI 1.00-3.36) respectively. A similar association of LTL with progression was also observed. These results suggest that shorter LTL was associated with aggressive prostate cancer at diagnosis and may predict worse prognosis.