Clinical implications of TMPRSS2-ERG fusion in African American men with localized prostate cancer

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Background: Recent studies demonstrate that the prevalence of TMPRSS2-ERG fusion in prostate tumors varies by ethnicity: The majority of African-American men (AAM) have ERG-negative tumors while the majority of non-African-American men (NAAM) have ERG-positive tumors. However, the clinical implications of the disparity in TMPRSS2-ERG fusions and ERG expression are not understood. We evaluate the impact of ERG expression by ethnicity on prostate cancer (PCa) clinical outcomes.

Methods: Using the Study of Clinical Outcomes, Risk, and Ethnicity (SCORE) study, we identified PCa patients who underwent prostatectomy between 1991 - 2012. Immunohistochemical stain for ERG was performed on FFPE tissue to study the incidence and pattern of TMPRSS-ERG fusion in PCa of 200 men who were matched on PSA, pathologic Gleason grade, and T-stage. Analysis of homogeneous and heterogeneous express of ERG within each PCa was performed. We then evaluated the effect of heterogeneity of ERG expression on clinical outcomes including pathologic T3 disease (pT3) and biochemical failure (BF).

Results: Clinical and pathologic characteristics were similar between ethnicity except for a higher prevalence of positive surgical margins in NAAM compared to AAM (35% vs 21%; p=0.03). Prevalence of ERG biomarker expression was lower in AAM vs. NAAM (32% vs 47%, p=0.04). Higher pathologic Gleason sum of >7 (3+4) was associated with ERG-negative status as compared to ERG-positive (homogenous and heterogeneous) status (29.1% vs 10.8% vs 8.6%; p=0.04). Heterogeneous expression of ERG was observed in 51.4% of ERG-positive cases. The incidence of ERG heterogeneity was higher in AAM as compared with NAAM (69% vs 35%; p=0.005). Among NAAM, ERG expression heterogeneity predicted increased pT3 disease (OR: 4.5, CI: 1.2 to 17.2, p=0.02). A non-significant difference in the opposite direction was observed for AAM (OR: 0.21, CI: 0.04 to 1.1, p=0.07). There was no significant correlation between ERG-negative tumors and pT3 disease. On multivariate analysis, AAM with ERG-negative tumor status trended towards worse 3-year BF in AAM (HR: 3.4, CI: 0.99-11.39, p=0.05). ERG-status did not impact biochemical outcomes in NAAM.

Conclusion: The majority of prostate tumors from AAM do not express ERG. ERG-positive tumors in AAM show a predominantly heterogeneous expression pattern associated with pT3 disease in an ethnic-dependent manner. We observed a trend towards worse 3-year BF in AAM with ERG-negative tumors. These results suggest that ERG might play a different role in the pathogenesis of PCa in AAM compared with NAAM.

Conflict of interest: None

Funding:

This work was funded in part by PHS grants R01-CA085074, P50-CA105641, P60-MD-006900 (to T.R.R.), and DOD grant PC-121189, and the Prostate Cancer Foundation Young Investigator Award (to K.Y.).