

614 Morphological and molecular pathway-based analysis of Gleason score 7 prostate cancer using a 17-gene expression assay

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Introduction & Objectives

Adverse outcomes associated with Gleason Score 7 (GS7) prostate biopsies have been correlated with increasing amounts of Gleason Pattern 4 (GP4) and certain morphologic subtypes. The Genomic Prostate Score (GPS) is a 17-gene biopsy-based RT-PCR assay analytically and clinically validated as an independent predictor of Adverse Pathology (AP) at prostatectomy and Biochemical Recurrence (BCR) (Eur.Urol 68(1):123-31, 2015). The GPS comprises genes from four gene pathways (androgen signalling, stromal response, cellular organization, and proliferation) that together were shown to discriminate cancer aggressiveness beyond individual gene pathways.

Material & Methods

5,000 prostate biopsies submitted for a GPS were centrally reviewed for GS, %GP4, and GP4 morphologic subtype. The GPS assay was performed and individual gene pathway scores were examined along with the composite GPS for all cases with GS7.

Results

23% (n=1143) of biopsies were GS7, 20% (n=1005) were GP3+4 (<10% GP4: 64%, 10-25% GP4:20%, and 26-50% GP4:16%) and 3% (n=138) were GP4+3. Poorly Formed Glands (PFG) was the predominant morphology (54%, n=619), followed by Fused Glands (FG) (24%, n=270), cribriform (19%, n=214), and glomeruloid (3%, n=40). The median GPS for all GS7 biopsies was 31 (IQR 23-41). Cribriform morphology had the highest median GPS 34 (IQR 26-44), followed by PFG 32 (IQR 24-41), FG 30 (IQR 22-40), and glomeruloid 25 (IQR 20-32). The median GPS values were 22 (IQR 16-29), 29 (IQR 22-38), 33 (IQR 26-43), 35 (IQR 27-46), and 37 (IQR 27-47) for men with a percentage GP4 of 0%, <10%, 10-25%, 26-50%, and >50%, respectively. Variations between individual gene pathway scores among each %GP4 category and each GP4 morphology were reflected in the wide range of GPS values and wide range of estimated risk of AP and BCR in all biopsies with GS7. Increasing percentages of GP4 were associated with decreased androgen signalling and cellular organization scores and increased stromal response and proliferation scores. Gene expression pathways varied among GP4 morphologies with the cribriform pattern showing the lowest cellular organization and highest proliferation scores and the PFG pattern showing the highest stromal response and lowest androgen signalling scores.

Conclusions

The GPS assay highlights a broad spectrum of tumour aggressiveness in a series of 1143 biopsies containing different GP4 morphologic subtypes and percent GP4. Variation within individual gene expression pathways suggest measurable underlying biologic differences among GS7 prostate cancer may contribute to an increased risk of AP and BCR.