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The Impact of a Biopsy Based 17-Gene Genomic Prostate Score on Treatment Recommendations in Men with Newly Diagnosed Clinically Prostate Cancer Who are Candidates for Active Surveillance

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Abstract

Introduction: The biopsy based 17-gene GPS was clinically validated to predict the likelihood of adverse surgical pathology in men with NCCN® very low, low or low-intermediate risk prostate cancer. We performed a prospective study to assess the impact of incorporating GPS into treatment recommendations in 3 high volume urology practices.

Methods: Men with newly diagnosed prostate cancer meeting specific NCCN criteria were prospectively enrolled in the trial. Biopsy tissue was analyzed. Urologists indicated treatment recommendations on questionnaires administered before and after GPS. The primary study objectives were to assess all changes in treatment modality and/or treatment intensity after GPS.

Results: A total of 158 men were included in analysis, including 35, 71 and 52 at NCCN very low, low and low-intermediate risk. Biological risk predicted by GPS differed from NCCN clinical risk alone in 61 men (39%). Overall 18% of recommendations between active surveillance and immediate treatment changed after GPS. The relative increase in recommendations for active surveillance was 24% (absolute change 41% to 51%). In 41 of 158 men (26%) modality and/or intensity recommendations changed after GPS, including 25, 14 and 2 in whom recommendation intensity decreased, increased and were equivocal, respectively. All changes were directionally consistent with GPS. The NCCN low risk group showed the greatest absolute recommendation change after GPS (37%). In 17 of 57 men (30%) the initial recommendation of radical prostatectomy was changed to active surveillance after GPS. Urologists indicated greater confidence and found that incorporating GPS was useful in 85% and 79% of cases, respectively, including when biological risk confirmed the clinical risk category.

Abbreviations and Acronyms

ADT = androgen deprivation therapy

AS = active surveillance

Columbia = New York-Presbyterian Hospital, Columbia University

DVU = Delaware Valley Urology, LLC

EBRT = external beam radiation therapy

GP = Gleason pattern

GPS = Genomic Prostate Score

GS = Gleason score

LN = lymph node

OCU = Orange County Urology

PCa = prostate cancer

PSA = prostate specific antigen

RP = radical prostatectomy

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Conclusions: This study demonstrates that the 17-gene GPS influenced treatment recommendations among urologists and provided increased confidence in these recommendations in patients at NCCN very low to low-intermediate risk.

Key Words: prostatic neoplasms, biological markers, risk assessment, molecular diagnostic techniques

There is growing consensus that many PCa cases diagnosed in the PSA screening era are biologically insignificant and could be managed by AS. However, most men diagnosed with early stage PCa receive immediate treatment.[1] While use of AS appears to be increasing,[1] there is uncertainty among clinicians regarding the accuracy of current assessment tools to identify low risk disease.[2] Biopsy GS is a strong independent predictor of risk. However, 30% to 40% of cases show discordance between biopsy and prostatectomy GS due to inherent tumor heterogeneity and the under sampling associated with conventional biopsy techniques.[3–5] Clearly biomarkers could help improve risk stratification in men with newly diagnosed PCa.

The 17-gene GPS assay (Oncotype DX®) is a biopsy based genomic test specifically developed to discriminate clinically indolent from aggressive PCa while accounting for tumor heterogeneity and multifocality.[6] The assay was analytically validated and can be performed on the small amounts of RNA recoverable from fixed, paraffin embedded needle biopsy tissue.[7] The assay result is GPS, a continuous score on a scale of 0 to 100 on which higher GPS represents more aggressive disease.[6] GPS was clinically validated in 395 patients with PCa who underwent prostatectomy but who would have been candidates for AS.[6] The study showed that GPS was an independent predictor of high grade and/or high stage (pT3) disease at surgery. For every 20-unit increase in GPS the likelihood of adverse surgical pathology essentially doubled even after adjusting for other clinical characteristics such as NCCN risk (OR 1.9, 95% CI 1.3–2.8, $p < 0.001$) or UCSF-CAPRA (University of California-San Francisco Cancer of the Prostate Risk Assessment) score (OR 2.1, 95% CI 1.4–3.2, <0.005, respectively). By providing more accurate risk stratification GPS provided quantitative information that can be used to expand the pool of patients at low risk who are suitable candidates for AS and identify those who would benefit from immediate treatment.[6]

This clinical utility study was designed to assess the GPS impact on treatment recommendations in men newly diagnosed with NCCN[8] very low, low or low-intermediate risk PCa. We compared treatment recommendation changes after GPS by NCCN risk group. We also evaluated physician confidence in their recommendations after receiving the GPS result in academic and community based urology practice settings.

Materials and Methods

Study Objectives

The primary objectives were to describe 1) the overall proportion of patients in whom urologists changed recommendations between immediate treatment and AS after receiving the GPS result, and 2) all changes in treatment modality and intensity after receiving the result. Treatment intensity changes were defined as an increase (from AS to any immediate treatment, or any increase in the extent of planned LN dissection at RP or from any single therapy to multimodal therapy), a decrease (from multimodal to any single therapy, from any immediate treatment to AS or a decrease in the extent of planned LN dissection at RP) or equivocal (a change between EBRT and RP or any other single therapy). Multimodal therapy included RP plus EBRT, RP plus ADT, EBRT plus ADT and EBRT plus brachytherapy. Urologists were also asked to describe their confidence in their treatment recommendations and the perceived utility of the assay via a questionnaire.

Site Selection and Patient Eligibility

Participating physicians were practicing urologists experienced with making primary treatment recommendations in patients with localized, clinically low risk PCa (NCCN very low, low or low-intermediate risk) (see Appendix).[8] The study was performed at 3 sites where comprehensive treatment options are offered, including 1 academic and 2 community based urology practices.

Patients eligible for study included men newly diagnosed (within the past 6 months) with very low, low or low-intermediate risk PCa and who were 50 years old or older with greater than 10-year life expectancy as determined by Social Security actuarial tables and the ability to provide informed consent. Patients with dominant GP 4 or any GP 5 disease on biopsy, NCCN high risk or NCCN locally