Genomic Scores are Independent of Disease Volume in Men with Favorable Risk Prostate Cancer: Implications for Choosing Men for Active Surveillance

Yaw A. Nyame,*,† Dominic C. Grimberg,† Daniel J. Greene, Karishma Gupta, Ganesh K. Kartha, Ryan Berglund, Michael Gong, Andrew J. Stephenson, Cristina Magi-Galluzzi and Eric A. Klein‡

From the Department of Urology, Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, Ohio

Abbreviations and Acronyms

GPS = Genomic Prostate Score™

GrdGrp = Gleason grade group

LFP = likelihood of favorable pathology

LR = low risk

NCCN® = National Comprehensive Cancer Network®

PSA = prostate specific antigen

PSAD = PSA density

VLR = very LR

Accepted for publication September 11, 2017.

* Correspondence: Department of Urology, Glickman Urological and Kidney Institute, Cleveland Clinic, 9500 Euclid Ave., Cleveland, Ohio 44195 (telephone: 216-444-2200; FAX: 216-445-2267; e-mail: nyamey@ccf.org).

† Equal study contribution and first authors.

‡ Financial interest and/or other relationship with Genomic Health.

Purpose: We sought to determine whether disease volume at prostate biopsy would correlate with genomic scores among men with favorable risk prostate cancer.

Materials and Methods: We identified all men with NCCN® (National Comprehensive Cancer Network®) very low and low risk disease who underwent Oncotype DX® prostate testing at our institution from 2013 to 2016. Disease volume was characterized as the percent of positive cores, the number of cores with greater than 50% involvement, the largest involvement of any single core and prostate specific antigen density. Nonparametric testing was performed to compare the median Genomic Prostate Score™ and the likelihood of favorable pathology findings between quartiles of disease volume.

Results: We identified 112 (37.8%) and 184 men (62.2%) at NCCN very low and low risk, respectively. Median scores did not differ significantly between disease volume quartiles (all $p > 0.05$). However, the median likelihood of favorable pathology findings statistically differed between volume quartiles (all <0.05). Seven of the 105 men (6.3%) with very low risk disease were reclassified at low risk and 13 of 181 (7.2%) with low risk disease were reclassified at intermediate risk. Genomic disease reclassification did not depend on biopsy tumor volume.

Conclusions: In patients with NCCN very low and low risk prostate cancer genomic scores did not demonstrate meaningfully significant differences by volume based on clinically established cutoff points. Moreover, genomic scores identified and reclassified men with higher risk disease despite generally acceptable surveillance characteristics in this group according to grade and volume. This suggests that in patients at low risk the tumor biological potential measured by genomics rather than by volume should inform decisions on active surveillance candidacy.

Key Words: prostatic neoplasms; watchful waiting; genomics; risk factors; pathology, surgical

Disease volume at prostate biopsy has been a key component of defining favorable risk prostate cancer as established by the landmark publication by Epstein et al.[1] Since that time, the definition of VLR prostate cancer has specified a low volume of disease at diagnosis based on 2 or fewer involved cores, maximum core involvement less than 50% and PSAD less than 0.15 ng/ml/gm. This definition, commonly known as the Epstein

0022-5347/18/1992-0438/0
THE JOURNAL OF UROLOGY®
© 2018 by American Urological Association Education and Research, Inc.
https://doi.org/10.1016/j.juro.2017.09.077
Vol. 199, 438-444, February 2018
Printed in U.S.A.

criteria, is used at many institutions to define candidates for active surveillance.[2] However, due to the inherent risk of sampling errors with needle biopsy the absence of these adverse features at biopsy does not guarantee favorable pathology findings at eventual radical prostatectomy.[1] Furthermore, despite long-term evidence of the safety of active surveillance in most men with pure GrdGrp 1 (ie Gleason score 3 + 3) tumors[3,4] violation of the Epstein criteria based on tumor volume has been used to exclude men against the recommendation for surveillance in some provider and institutional protocols.[5]

The diagnostic inaccuracies of biopsy and traditional risk stratification measures create a need for improved methods to identify men at low risk for progression who may avoid initial therapy. This limitation is being addressed by the growing use of genomic biomarkers[6–8] and multiparametic magnetic resonance imaging as diagnostic tools.[9,10] Oncotype DX® GPS is a 17-gene quantitative reverse transcriptase-polymerase chain reaction assay of select genes from 4 cancer related molecular pathways, including androgen signaling, cellular organization, stromal response and cellular proliferation.[11] It has been analytically[11] and clinically[12,13] validated when measured on prostate biopsies to predict adverse pathology (GrdGrp 3 or higher or nonorgan confined disease) as well as time to biochemical recurrence and metastasis.[14] Further, GPS testing in a clinical setting demonstrated an increase in the recommendation for and adoption of active surveillance in patients with newly diagnosed prostate cancer.[15] This led to a recommendation in the current NCCN® guidelines to consider such tests when qualifying men for active surveillance.[16]

In this study we determined prostate biopsy GPS scores and accompanying estimates of the likelihood of favorable pathology in men with Gleason grade group 1 (Gleason score 3 + 3) tumors as a function of tumor volume. Our purpose was to determine whether some men who did not meet traditional Epstein criteria would be safe candidates for active surveillance based on the molecular rather than the histological features of the tumors.

MATERIALS AND METHODS

All men at our institution who underwent GPS testing performed on prostate biopsy samples to aid in clinical decision making were identified from a genomic database. Men were excluded from analysis if they had NCCN intermediate risk disease.[16] In 36 men, including 19 at LR and 17 at VLR, core biopsy samples were submitted for genomic testing but failed to provide enough quality RNA for analysis. A total of 296 men biopsied between 2013 and 2016 were included in analysis. Institutional review board approval was obtained for this study.

Clinical Data

We reviewed the electronic medical record and a prospectively maintained active surveillance database to obtain all relevant demographic and clinical data, including patient age at biopsy, ethnicity/race, body mass index, initial PSA, digital rectal examination findings and followup duration. We also collected biopsy data, including Gleason score, prostate volume on transrectal ultrasound, the total number of cores taken, the number of positive cores, the number of cores with greater than 50% involvement and the largest percent of core involvement. Men were stratified into NCCN VLR and LR disease based on baseline data according to NCCN guidelines.[16] Disease volume was defined as 1) the percent of positive cores, 2) the number of cores with greater than 50% involvement, 3) the largest involvement of any single core and 4) PSAD. Data on GPS and associated LFP, and the estimated probability of low grade (GrdGrp 1 or 2) and organ confined (pT2) disease were obtained from the Oncotype DX test result of each patient.

As mentioned, GPS is a 17-gene quantitative reverse transcriptase-polymerase chain reaction assay of select genes from 4 cancer related molecular pathways, including androgen signaling, cellular organization, stromal response and cellular proliferation. Testing is performed on tissue obtained from core prostate biopsies. LFP is the 0% to 99% probability reported in the initial iterations of the GPS test result. A calculation predicts the probability of adverse biological disease compared to that in men in a similar NCCN risk group.

Biopsy core number and location were determined according to physician preference and were not standardized. All biopsies were reviewed at our institution by expert genitourinary pathologists in accord with current ISUP (International Society of Urological Pathology) criteria.[17]

Statistical Methods

Descriptive statistics were performed to characterize the cohort. Data are presented as the median and IQR for continuous variables, and the frequency and proportion for categorical variables. The primary end point of this study was to compare the likelihood of favorable pathology (organ confined and with no primary Gleason pattern 4 or 5) between patients stratified by disease volume as estimated by the 3 mentioned volume parameters. Secondary end points included subanalysis to assess the rate of disease reclassification using GPS. Each volume parameter was divided into statistical quartiles with cutoff points at the 25th, 50th and 75th percentiles.

The Kruskal-Wallis test was used to compare median LFP among quartiles of each volume parameter. The Mann-Whitney U test was applied for tests between only 2 groups. All statistical tests were 2-sided with significance defined at $p < 0.05$. Statistical analyses were performed using Stata®, version 12.1 and IBM® SPSS®, version 24.

RESULTS

Table 1 lists baseline cohort clinical and demographic data. In the cohort 112 (37.8%) and 184 men (62.2%) had NCCN VLR and LR prostate

Download English Version:

https://daneshyari.com/en/article/8771602

Download Persian Version:

https://daneshyari.com/article/8771602

Daneshyari.com