Utilization of ExoDx™ Prostate Test for Prostate Cancer Risk Stratification in the African American Population

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Introduction

Prostate cancer (PC) affects men of all races but is particularly concerning among African American (AA) men. AA men are not only more likely to be diagnosed with prostate cancer but also tend to have more aggressive forms of the disease at every stage, from prevention and screening to clinical outcomes, which calls for a focused approach to early detection and effective treatment options.[1] The ExoDx Prostate (EPI) Test is a non-invasive urine test for assessing risk of high-grade prostate cancer (HGPC) currently used in shared decision-making for men considering diagnostic prostate biopsy. The 15.6 cut-point was selected by a committee of urology key opinion leaders as to what risk would be tolerated to avoid unnecessary biopsies (>90% NPV) without missing clinically significant ≥GG2 PC.

Methods

A large level 1 evidence clinical trial[2] conducted in 2017 (Prostate Biopsy Decision Impact Trial) also known as the Clinical Utility study enrolled 942/1094 subjects with usable data being considered for initial biopsy, to either receive an EPI test result as part of their biopsy decision process or to proceed with standard of care (SOC). This report is based on the follow-up data at 2.5 years post-trial enrollment, by assessing patient outcomes over time through analysis of subsequent changes in biopsy decisions and timing as well as the resultant pathology. Patients were eligible irrespective of race or ethnicity. There was a high representation of African American patients in this study (~23%). Eligible patients were male, aged ≥50 years with clinical indication of PC based on an elevated PSA (2–10 ng/mL) without clinical history of prior negative biopsy. Men with a history of invasive treatment for benign prostatic disease within six months or taking medications affecting PSA levels within 3–6 months were excluded. After 2.5 years, 833/942 subject records were assessed for outcomes based on the pre-biopsy EPI score in the ongoing 5-year follow-up of the trial, and a subset of 186 African American out 833 subjects were also evaluated.

Results

AA men in the EPI arm and SOC arm were 21.7% (89/411) and 23% (97/422) respectively. This was consistent with the Clinical Utility study. For AA men, 41.6% (37/89) were diagnosed with HGPC in the EPI arm compared to 29.9% (29/97) in the randomized SOC arm. Over the 2.5-year follow-up period, significantly more HGPC was detected in the EPI arm as compared to the SOC control arm. EPI had an impact on the decision to biopsy in the EPI arm. More EPI positive (high-risk) subjects underwent biopsy in the EPI arm compared to the SOC arm, hence more HGPC was detected in the EPI arm. This real-world study demonstrated the EPI test improved quality of care by improving compliance, and more appropriately deferring low-risk men from having a prostate biopsy and referring higher-risk men to biopsy. The biopsy rate in the EPI high-risk (EPI positive) group is significantly higher than the low-risk (EPI negative) group from the EPI arm (p=0.01). The SOC arm had an EPI test score blinded to the doctor and patient. The EPI high-risk (EPI positive) and EPI low-risk (EPI negative) patients in the SOC arm had the same biopsy rates (p=0.25), indicating that EPI provides independent value to risk stratify these patients beyond SOC.

Table 1

AA Biopsy & HGPC rate - Clinical Utility Study

Clinical Utility study	EPI Arm EPI>15.6 (n=93)	EPI Arm EPI≤15.6 (n=9)	SOC Arm EPI >15.6 (n=100)	SOC Arm EPI≤ 15.6 (n=15)
Biopsy rate	68 (73.1%)	0 (0%)	40 (40%)	6 (40%)
Benign	19 (20.4%)	-	9 (9%)	3 (20%)
GG1	20 (21.5%)	-	17 (17%)	1 (6.7%)
GG2	17 (18.3%)	-	5 (5%)	1 (6.7%)
GG3	7 (7.5%)	-	6 (6%)	1 (6.7%)
GG4	4 (4.3%)	-	0 (0%)	0 (0%)
GG5	1 (1.1%)	-	3 (3%)	0 (0%)
GG≥2	29 (31.2%)	-	14 (14%)	2 (13.3%)
GG≥3	12 (12.9%)	-	9 (9%)	1 (6.7%)

Table 2

AA Biopsy & HGPC rates - 2.5 year follow-up

2.5 year follow-up	EPI Arm EPI>15.6 (n=83)	EPI Arm EPI≤15.6 (n=6)	SOC Arm EPI >15.6 (n=83)	SOC Arm EPI≤ 15.6 (n=14)
Biopsy rate	71 (85.5%)	3 (50%)	52 (62.7%)	11 (78.6%)
Benign	23 (27.7%)	1 (16.7%)	15 (18.1%)	5 (35.7%)
GG1	12 (14.5%)	1 (16.7%)	13 (4.5%)	1 (21.4%)
GG2	20 (24.1%)	1 (16.7%)	12 (8.4%)	3 (14.3%)
GG3	9 (10.8%)	0 (0%)	7 (6%)	2 (6.7%)
GG4	4 (4.8%)	0 (0%)	2 (2.4%)	0 (0%)
GG5	3 (3.6%)	0 (0%)	3 (3.6%)	0 (0%)
GG≥2	36 (43.4%)	1 (16.7%)	24 (28.9%)	5 (35.7%)
GG≥3	16 (19.3%)	0 (0%)	12 (14.5%)	2 (14.3%)

Table 1. The AA subset of the Clinical Utility study shows a significantly higher rate of biopsies performed and more HGPC (GG ≥ 2) found in the high-risk EPI group compared to the low-risk EPI group from the EPI arm (p<0.001 and p=0.02, respectively) .

Table 2. The AA subset in the 2.5-year follow-up data shows a significantly higher biopsy rate in the high-risk group from the EPI arm (p=0.01).

Figure 1

Consort Flow Diagram

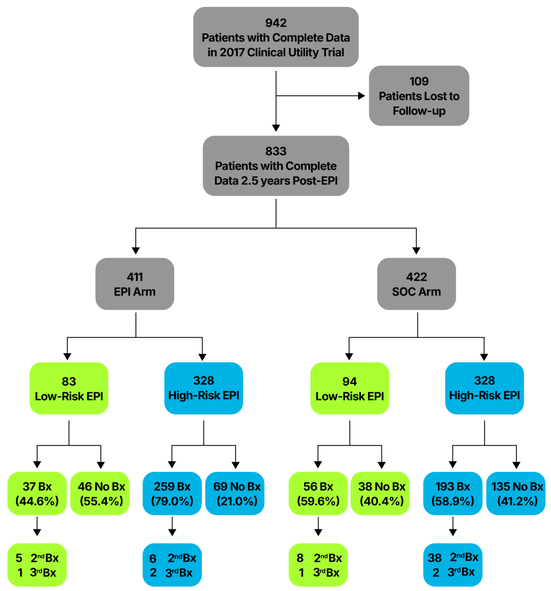

Figure 1. A total of 72 urologists from 24 clinical sites enrolled 942 patients for the study, of which 109 were lost to follow-up. Only the EPI arm received the initial EPI result back. Patients in the SOC arm did not receive the EPI result back, and instead relied on standard of care for all biopsy decisions at the time of enrollment, and throughout the 2.5-year follow-up.

Bx=Biopsy, EPI=ExoDx Prostate (IntelliScore), SOC=Standard of Care.

Figure 2

Biopsy Rates and HGPC Probability by EPI score in the study population (n=833) - 2.5 year follow-up and Clinical Utility Study

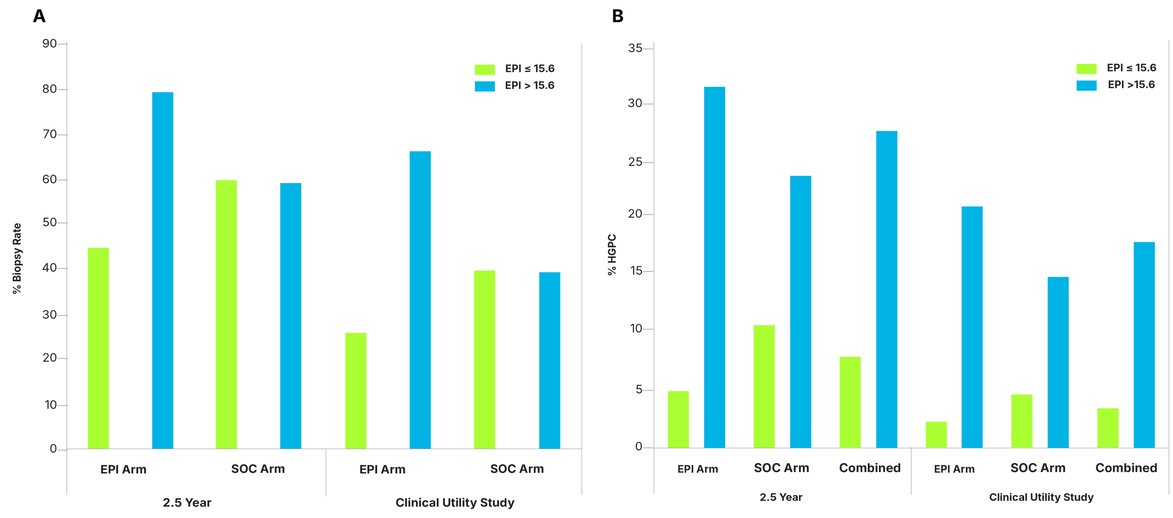

Figure 2. Comparison of biopsy rate and HGPC (≥GG2) in the randomized, EPI vs control (SOC) arm at time points of the Clinical Utility trial and 2.5 year follow-up.

A. Biopsy rate - In both, Clinical Utility study and the 2.5-year follow-up data, patients with low-risk EPI scores in the EPI arm had a significantly lower biopsy rate than patients with high-risk EPI scores, while patients in the SOC arm deferred biopsies at almost identical rates in the low and high-risk EPI score groups.

B. HGPC Probability - After the 2.5 years follow-up, patients with low-risk EPI scores had very low probability of a HGPC (≥GG2) diagnosis, while patients with high-risk EPI scores had much higher probability of HGPC diagnosis, regardless of the study arm.

This was consistent in the Clinical Utility study data and in the 2.5-year follow-up data.

Both the Clinical Utility study and the 2.5-year follow-up data showed significantly lower biopsy rates in the low-risk EPI group. The probability of detecting HGPC (GG ≥ 2) in the EPI high-risk group was much higher regardless of the study arm.

The percentage of HGPC cancer found includes total patient number in the arm, including patients that did not receive a biopsy.

This study highlights the impact of a pre-biopsy EPI score and how it changes the clinical outcome for patients when compared to a blinded control arm that could utilize any standard of care parameters, including other biomarkers. The original blinded randomized study showed that nearly twice as many HGPC cases were found when EPI was utilized in the AA population compared to standard of care (29 vs 16) (p=0.004).

Even after 2.5 years of follow-up[3], the AA patient cohort that received a single pre-biopsy EPI result still identified more HGPCs compared to the AA standard of care arm (37 vs 29). This is consistent with the outcome in the total study population. Because more biopsies were done in the EPI low-risk SOC arm group, 4 more HGPCs were detected after 2.5 years as compared to the EPI low-risk EPI arm group in the AA cohort.

Evaluation of the AA population subset of this study demonstrates that a pre-biopsy EPI test leads to stratification of high-risk vs low-risk prostate cancer in patients and enables the detection of more HGPC. This is consistent even 2.5 years after the initial biopsy decision-making process.

In summary, incorporation of the EPI test directing appropriate patients to biopsy identified more HGPC, including in the AA cohort.

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2. Tutrone R, Donovan MJ, Torkler P, et al. Clinical utility of the exosome based ExoDx Prostate (IntelliScore) EPI test in men presenting for initial Biopsy with a PSA 2-10 ng/mL. Prostate Cancer Prostatic Dis 2020 234. 2020;23(4):607-614.
3. Tutrone, R., Lowentritt, B., Neuman, B. et al. Correction to: ExoDx prostate test as a predictor of outcomes of high-grade prostate cancer – an interim analysis. Prostate Cancer Prostatic Dis (2023). https://doi.org/10.1038/s41391-023-00681-3