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Original article

Fusion prostate biopsy outperforms 12-core systematic prostate biopsy in patients with prior negative systematic biopsy: A multi-institutional analysis

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Abstract

Introduction and objectives: Patients with persistently elevated prostate specific antigen (PSA) and prior negative 12-core TRUS prostate biopsy (or biopsies) (systematic biopsy—SBx) are a diagnostic challenge. Repeat SBx or saturation biopsy in this cohort has been shown to have an even lower yield. The aim of our study is to compare the prostate cancer yield of magnetic resonance imaging (MRI) fusion biopsy (FBx) to SBx in a multi-institutional cohort comprised of patients with prior negative biopsies.

Methods: A multi-institutional review was performed on patients with a history of one or more prior negative SBx who underwent multiparametric MRI (mpMRI), followed by FBx and SBx in the same session. Imaging protocol was standardized across institutions and institutional genitourinary radiologists and pathologists reviewed mpMRI and pathology, respectively. Gleason score (GS) distribution and risk classifications were recorded. Prostate cancer with GS $\geq 3 + 4$ was defined as clinically significant (CS). Univariate and multivariable logistic regression was done to identify predictors of cancer detection on SBx and FBx.

Results: Seven-hundred seventy-nine patients from four institutions were included in the study. Median age and prostate specific antigen (IQR) were 63.1 (58.5–68.0) years and 8.5 (5.9–13.1) ng/dl, respectively. Median number of prior negative biopsies (range) was 2.0 (1–16). The cancer detection rate (CDR) in the cohort was 346/779 patients (44.4%). Total CS CDR was 30.7% (239/779 patients), with FBx detecting 26.3% (205/779) of patients with CS disease and SBx diagnosing an additional 4.4% (34/779) of patients ($P < 0.001$). Furthermore, of all cancers detected by each modality, FBx detected a higher proportion of CS cancer compared to SBx (one negative biopsy: 75 vs. 50%, $P < 0.001$, 2–3 negative biopsy: 76 vs. 61%, $P = 0.006$, 4 or more negative biopsies: 84 vs. 52%, $P = 0.006$). As such, SBx added a relatively small diagnostic value to FBx for detecting CS disease (one negative biopsy 3.5%, 2–3 negative biopsies 5%,

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4 or more negative biopsies: 1%). FBx also outperformed SBx for upgrading patients to an intermediate or high-risk cancer category (GS > 6) (one negative biopsy 11.5% vs. 3.6%, 2–3 negative biopsy 10.3% vs. 5.3%, 4 or more negative biopsies 19.1% vs. 1.1%). On multivariable analysis, the number of prior negative biopsies was a significant negative predictor of CS CDR on SBx ($P = 0.006$), but not on FBx ($P = 0.151$).

Conclusions: Using a large multi-institutional cohort, we were able to demonstrate that FBx outperformed SBx in patients with prior negative systematic biopsy. This was due, in part, to the decreasing CS CDR by SBx with increased number of prior biopsies. The yield of FBx stayed constant and did not decrease with increased number of prior negative biopsies. Therefore, repeat SBx alone in patients with multiple prior negative biopsies will be hindered by lower yield and FBx should be utilized concurrently in these patients.

Keywords: Prostate cancer; Multiparametric MRI; Fusion biopsy; Prior negative biopsy; Systematic biopsy

1. Introduction

In men with suspicion of prostate cancer including elevated prostate specific antigen (PSA) or abnormal digital rectal exam, or both, systematic 12-core transrectal ultrasound-guided biopsy (systematic biopsy—SBx) has traditionally been a principal method of diagnosing prostate cancer. However, SBx suffers from overdiagnosis of clinically insignificant cancer, underdiagnosis of clinically significant (CS) cancer, and has a high false negative rate as ultrasound alone lacks sufficient discriminative ability [1–3]. Patients with continued suspicion of prostate cancer and negative SBx are a diagnostic challenge and around 38% will undergo repeat SBx over 5 years in an effort to obtain a diagnosis [4]. Unfortunately, repeating SBx has little efficacy in identifying cancerous lesions, with only 10% to 25% cancer detection rate (CDR) even after the fourth repeat SBx [5]. Moreover, the diagnostic yield of CS disease relative to insignificant cancer is low and continues to decline with each subsequent biopsy session [6]. As such, these multiple re-biopsies lead to increased cost, delay in diagnosis and added patient morbidity.

Multiparametric magnetic resonance imaging (mpMRI) fusion biopsy (FBx) has emerged as a promising alternative and addition to SBx in the detection of CS cancer because of its higher propensity to detect CS disease, while decreasing the detection of insignificant disease, relative to SBx [7–10]. Several single-institution studies have previously demonstrated the benefit of FBx in detecting prostate cancer in patients with prior negative biopsies [1,11]. However, the analysis of FBx cancer detection as a function of the number of prior negative SBxs was limited in previous studies.

The aim of our study was twofold. First, we sought to investigate the efficacy of FBx relative to SBx in the detection of CS prostate cancer using a multi-institutional cohort comprised of patients with prior negative biopsies. Secondly, within this cohort, we wanted to ascertain the independent effect that number of prior negative biopsies had on FBx and SBx cancer detection, respectively.

2. Methods

2.1. Study population

A retrospective review of prospectively maintained databases of patients who underwent initial mpMRI followed by MRI-TRUS fusion-guided biopsy and systematic 12-core biopsy for prostate cancer suspicion at participating institutions was performed. Patients were enrolled at the following four institutions: National Cancer Institute, Bethesda, MD, Northwell Health, New Hyde Park, NY, University of Alabama at Birmingham School of Medicine, Birmingham, AL and SUNY Upstate Medical University, Syracuse, NY. Patients without a diagnosis of cancer, who had a suspicious prostate lesion on imaging and had a history of one or more prior negative SBx were included in this study. If patients received multiple mpMRI studies or FBxs during this time period or both, only the first session was included for analysis. Institutional review board approval was obtained at each institution.

2.2. Image acquisition and interpretation

mpMRI consisted of triplanar T2 weighted, diffusion weighted imaging and dynamic contrast imaging. All studies met the minimum criteria as outlined by the Prostate Imaging-Reporting and Data System: 2015, Version 2 (PIRADSv2) [12]. Each institution's respective uroradiologists reviewed the imaging.

2.3. Biopsy Protocol

Patients who had suspicious areas identified on mpMRI underwent both SBx and FBx in the same session utilizing an office-based platform (UroNav, Philips/In Vivo Corp, Gainesville, FL, USA). In addition to the systematic 12-core biopsy, at least 2-targeted cores were obtained per target pre-identified on mpMRI by the uroradiologist. Biopsy specimens were evaluated and assigned with Gleason scores (GS) by the pathologists at the respective institutions.