

Clinical Findings and Treatment Outcomes in Patients with Extraprostatic Extension Identified on Prostate Biopsy



Katherine Fleshner, Melissa Assel, Nicole Benfante, Justin Lee, Andrew Vickers, Samson Fine, Sigrid Carlsson and James Eastham*

From the McGill University (KF), Montreal, Quebec, Canada, Departments of Epidemiology and Biostatistics (MA, AV, SC), Pathology (SF) and Surgery (SC) and Urology Service, Department of Surgery (NB, JL, JE), Memorial Sloan Kettering Cancer Center, New York, New York, and Department of Urology, Institute of Clinical Sciences, Sahlgrenska Academy at University of Göteborg (SC), Göteborg, Sweden

Purpose: We describe histopathological, clinical and imaging findings among men with extraprostatic extension on prostate biopsy.

Materials and Methods: We searched our institutional pathology database between 2004 and 2015 for pathology reports detailing extraprostatic extension on prostate biopsy in untreated patients. Patient characteristics, biopsy features, imaging interpretations and outcomes were examined.

Results: Of 19,950 patients with prostate cancer on biopsy 112 had extraprostatic extension for a prevalence of 0.6% (95% CI 0.5–0.7). Most of the 112 patients had palpable, high grade (Gleason score 9), high volume disease, which was classified as high risk in 34 (30%), locally advanced in 17 (15%) and metastatic in 39 (35%). Most patients had 1 or 2 cores with extraprostatic extension, typically at the base and with concomitant perineural invasion. Extraprostatic extension was identified by magnetic resonance imaging in 32 of 40 patients (80%). Median followup in those who did not die was 1.3 years (IQR 0.3–4.2). Outcomes in the subgroup of 24 men treated with radical prostatectomy were consistent with high risk disease, including positive margins in 14 (58%), seminal vesicle invasion in 10 (42%) and lymph node invasion in 11 (46%). In the entire cohort the 3-year risks of metastasis and overall mortality were 32% (95% CI 22–44) and 37% (95% CI 27–50), respectively. We did not find evidence to suggest that the proportion of cores with cancer that also had extraprostatic extension was associated with overall mortality ($p = 0.09$).

Conclusions: Extraprostatic extension is a rare finding on prostate biopsy. It is strongly associated with other features of aggressive prostate cancer.

Abbreviations and Acronyms

ADT = androgen deprivation therapy

EPE = extraprostatic extension

GS = Gleason score

JHU = The Johns Hopkins University

LNI = lymph node invasion

MRI = magnetic resonance imaging

MSKCC = Memorial Sloan Kettering Cancer Center

NCCN® = National Comprehensive Cancer Network®

PSA = prostate specific antigen

RP = radical prostatectomy

RT = radiation therapy

SVI = seminal vesicle invasion

Key Words: prostatic neoplasms, prostatectomy, biopsy, neoplasm invasiveness, mortality

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* Correspondence: Urology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, 353 East 68th St., New York, New York (telephone: 646-422-4322; e-mail: easthamj@mskcc.org).

EXTRAPROSTATIC extension on histopathological examination refers to the identification of tumor cells beyond the borders of the prostate. It is most often recognized as tumor intermingling with periprostatic adipose tissue. EPE can manifest focally throughout the tissue, that is only a few neoplastic glands are seen outside the prostate or EPE becomes nonfocal with more glands.¹ Although EPE is most commonly detected in the RP specimen, it can also be found on preoperative MRI and on prostate biopsy.²

EPE in the RP specimen is well studied. It is a critical part of the pathological tumor staging process as all RP specimens containing EPE are classified as pathological stage pT3.³ EPE found at RP is a risk factor for poor prognosis and, therefore, it is often included in postoperative nomograms predicting outcomes such as biochemical recurrence after RP.^{1,4} Sometimes adjuvant treatment is recommended upon detection.⁵

EPE can also sometimes be captured on MRI, which is used for staging purposes and treatment planning. MRI to detect EPE at surgical pathology has moderate 72% sensitivity and 65% specificity.⁶

Occasionally, EPE is also noted on the pathology report from the prostate biopsy. However, detecting it on prostate biopsy is fairly uncommon. To our knowledge only 1 publication in the literature describes outcomes in patients with EPE on prostate biopsy.² In that study, which was done at JHU, Miller et al examined 51,891 biopsies performed between 1997 and 2009, and reported an EPE prevalence of only 0.19%. Because of its rare occurrence, the clinical significance of this finding is not well understood. Little is known about whether biopsy detected EPE is an independent predictor of aggressive prostate cancer.

Therefore, we performed the current study for several reasons. We sought to 1) estimate the frequency of this occurrence among men with a positive prostate biopsy at our institution, 2) describe histopathological and clinical characteristics as well as outcomes and 3) compare the congruity of EPE detection on biopsy, MRI and RP specimens. We hypothesized that, using the current transrectal ultrasound guided biopsy technique, EPE would mainly be found at the base of the prostate.

MATERIALS AND METHODS

Selection Criteria

The current study was done after receiving institutional review board approval. Figure 1 shows the study cohort flowchart. Between the inception of the MSKCC institutional electronic pathology database in 2004 and the last followup on July 31, 2015 a total of 19,950 men with prostate biopsies positive for prostate cancer were

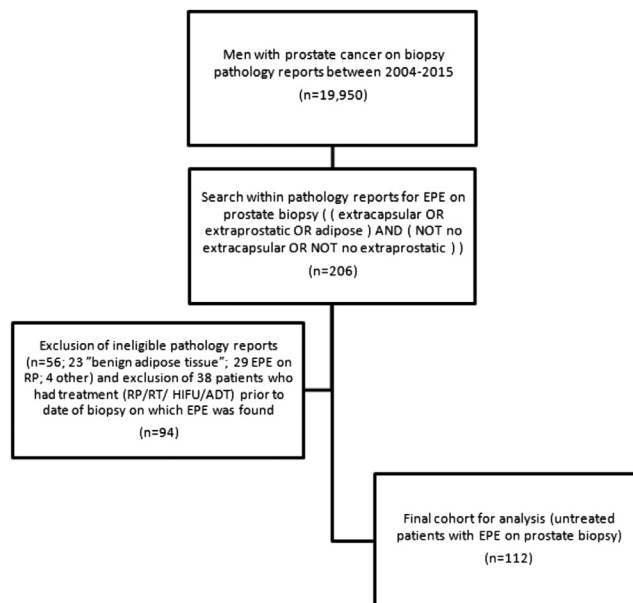


Figure 1. Cohort flow chart. *HIFU*, high intensity focused ultrasound.

recorded. Patients were seen at the urology clinic or by medical oncology or radiation oncology staff at our institution.

We performed a free text search for the words (extracapsular OR extraprostatic OR adipose) AND (NOT no extracapsular OR NOT no extraprostatic) in prostate biopsy pathology reports performed during this period, which retrieved 206 hits. Because tumor in the adipose tissue is per definition EPE and intraprostatic adipose tissue is extremely rare, we also included the word adipose. Pathology reports with benign adipose tissue and ineligible pathology reports caught by the search were excluded from analysis (fig. 1).

Since it is difficult to examine the irradiated or treated prostate under the microscope and our study questions relate to men without prior treatment, we excluded those whose date of therapy (ADT, radiotherapy, brachytherapy or high intensity focused ultrasound) preceded the date of biopsy. We also excluded men with a RP date preceding the date of biopsy who underwent biopsy of the prostate bed upon recurrence. This left a final count of 112 men available for analysis and 183 biopsy areas in patients with multiple biopsies showing EPE.

Since our institution is a referral center, the pathology report search identified several types of biopsies, including new biopsies performed at our institution, repeat biopsies that sought to corroborate the prostate cancer diagnosis from elsewhere and rereviewed reports by our pathologists of diagnostic biopsies performed elsewhere. Thus, patients presenting with distant metastasis who had confirmatory biopsies could be included in the search.

Statistical Analysis

The frequency of EPE on prostate biopsy was calculated as the prevalence of EPE from the pathology report search divided by the total number of men with biopsies positive

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