Biopsy Core Features are Poor Predictors of Adverse Pathology in Men with Grade Group 1 Prostate Cancer

François Audenet, Emily A. Vertosick, Samson W. Fine, Daniel D. Sjoberg, Andrew J. Vickers, Victor E. Reuter, James A. Eastham, Peter T. Scardino and Karim A. Touijer*

From the Departments of Urology (FA, JAE, PTS, KAT), Epidemiology and Biostatistics (EAV, DDS, AJV) and Pathology (SWF, VER), Memorial Sloan Kettering Cancer Center, New York, New York

Purpose: Active surveillance is often restricted to patients with low risk prostate cancer who have 3 or fewer positive cores. We aimed to identify predictors of adverse pathology results for low risk prostate cancer treated with radical prostatectomy and determine whether a threshold number of positive cores could help the decision process for active surveillance.

Materials and Methods: A total of 3,359 men with low risk prostate cancer underwent radical prostatectomy between January 2000 and August 2016. We analyzed the relationship between biopsy core features and adverse pathology at radical prostatectomy, defined as Grade Group 3 or greater, seminal vesicle invasion or lymph node involvement.

Results: Of the 171 cases (5.1%) with adverse pathology findings at radical prostatectomy 144 (4.3%) were upgraded to Grade Group 3 or greater, 31 (0.9%) had seminal vesicle invasion and 15 (0.4%) had lymph node involvement. Prostate specific antigen and patient age were the only predictors of adverse pathology results. There was no significant association with the number of positive cores, the total mm of cancer or the maximum percent of cancer in any core. When we expanded the definition of adverse pathology to include Grade Group 2 and extraprostatic extension, the association between core features and outcome was statistically significant but clinically weak, and with no evidence of threshold effects.

Conclusions: There is little basis for excluding patients with otherwise low risk prostate cancer on biopsy from active surveillance based on criteria such as the number of positive cores or the maximum cancer involvement of biopsy cores.

Abbreviations and Acronyms

AS = active surveillance
ASIST = Active Surveillance Magnetic Resonance Imaging Study
BCR = biochemical recurrence
EPE = extraprostatic extension
GrdGrp = Grade Group
LNI = lymph node involvement
MRI = magnetic resonance imaging
PCa = prostate cancer
PRIAS = Prostate Cancer Research International Active Surveillance
PSA = prostate specific antigen
RP = radical prostatectomy
SVI = seminal vesicle invasion

Key Words: prostatic neoplasms, neoplasm grading, prostatectomy, watchful waiting, clinical decision-making

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* Correspondence: Urology Service, Department of Surgery, Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan Kettering Cancer Center, 353 East 68th St., New York, New York 10065 (telephone: 646-422-4486; FAX: 212-988-0768; e-mail: touijerk@mskcc.org).

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PRACTICE guidelines recommend that patients with low risk PCa should be treated with AS.[1,2] The purpose of AS is to reduce overtreatment and attendant morbidity without compromising the opportunity to cure lethal disease.

The exact criteria used to determine eligibility for AS vary importantly. For instance, in a systematic review on AS Dall'Era et al reported that in 7 major AS series eligibility criteria were used that differed in clinical stage, biopsy grade, PSA and biopsy core features.[3]

Of the criteria used for AS the prognostic value of GrdGrp and stage are unambiguous[4,5] and there has been considerable study of PSA level.[6] To date there has been little research on the prognostic value of biopsy cores.

The goal of our study was to determine the relationship between the number of positive biopsy cores and the oncologic risk. In particular we were interested in evaluating the widely used criterion that patients with more than 3 positive cores or more than 50% cancer involvement in any 1 core should be referred for immediate treatment.[3]

MATERIALS AND METHODS

After obtaining institutional review board approval we retrospectively collected data on 3,359 men who had GrdGrp 1 (Gleason score 3 + 3 = 6) disease on biopsy and PSA 10 ng/ml or less, and underwent RP at our institution between January 2000 and August 2016. While 86% of biopsies before RP were done elsewhere, the pathology results of these biopsies were reviewed at our institution prior to surgery.

We aimed to evaluate the relationship between the amount of cancer present on biopsy and the risk of adverse pathology findings at RP for low risk PCa. Adverse pathology was defined as GrdGrp 3 or greater (Gleason score 4 + 3 = 7 or greater), SVI or LNI. The amount of cancer was defined in 3 ways, including the number of positive biopsy cores, the total mm of cancer on biopsy and the maximum percent of cancer in any biopsy core. We excluded EPE and GrdGrp 2 (Gleason score 3 + 4 = 7) from our adverse pathology criteria as we had previously reported that the oncologic outcome remained favorable in cases of preoperatively low risk PCa which were up staged to EPE or upgraded to GrdGrp 2 following RP.[7]

Using the Wilcoxon rank sum and Fisher exact tests we compared patient characteristics and the amount of cancer on biopsy between patients with and without adverse pathology findings at RP. To investigate whether the probability of adverse pathology increased significantly when there was a larger amount of cancer on biopsy, we plotted the probability of adverse pathology using LOWESS. As a sensitivity analysis we repeated all analyses using an alternate definition of adverse pathology that included GrdGrp 2 and EPE. We also performed a sensitivity analysis limited to patients who underwent biopsy or had all biopsy cores reviewed at our institution. All analyses were done with Stata®, version 13.

RESULTS

The supplementary table (http://jurology.com/) lists patient characteristics. Adverse pathology at RP was present in 171 of the 3,359 patients (5.1%) who had low risk PCa on biopsy. Of these 171 cases 144 (4.3%) were upgraded to GrdGrp 3 or greater, 31 (0.9%) showed SVI, 15 (0.4%) showed LNI and 17 (0.5%) had 2 or more adverse features. Of note, 77% of the 3,359 patients underwent lymph node dissection since we believe that it improves the accuracy of PCa staging even in those at low risk.

The 171 patients with adverse pathology findings at RP were significantly older than the rest of the cohort (median age 62 years, IQR 56–66 vs 59, IQR 54–63, $p < 0.0001$). These 171 patients had significantly higher PSA before RP than the rest of the cohort (median 5.8 ng/ml, IQR 4.5–7.1 vs 4.7, IQR 3.4–6.1, $p < 0.0001$). The median number of positive cores in the whole cohort was 2 (IQR 1–3). The number of positive cores did not significantly differ between patients with vs without adverse pathology ($p = 0.7$).

We tested whether there was a significant association between the amount of cancer on biopsy and the risk of adverse pathology results at RP. We found no evidence of an association between the number of positive cores ($p = 0.7$), the total mm of cancer in the biopsy ($p = 0.6$) or the maximum percent of cancer in any core ($p > 0.9$, see table). Although we did not observe any significant associations, we wanted to explore the possibility of nonlinearity or discontinuities that would suggest a threshold for AS eligibility. Figure 1 shows the probability of adverse pathology findings in all patients based on the number of positive cores, the total mm of cancer on biopsy and the maximum percent of cancer in any biopsy core. There was no obvious evidence of a threshold effect.

On sensitivity analysis we repeated the analyses to include patients with GrdGrp 2 and EPE. Of the 3,359 patients 1,691 (50%) were found to have adverse pathology findings at RP based on this expanded definition. The number of positive biopsy cores, the total mm of cancer on biopsy, the maximum percent of cancer in any core, GrdGrp 2 and EPE were significantly associated with the risk of adverse pathology (all $p < 0.0001$, see table). Figure 2 shows the risk of adverse pathology findings plotted against core features. Similar to our analyses that excluded GrdGrp 2 and EPE, there was no evidence to support commonly used thresholds such as 3 positive cores or maximum 50% core involvement and the risk of adverse pathology.