Prediction of Extraprostatic Extension in Men With Biopsy Gleason Score of 8 or Greater

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Purpose: Recent data have shown that high grade prostate cancer is a potentially surgically curable disease in properly selected patients. We assessed the ability of preoperative variables to predict extraprostatic extension in men with biopsy Gleason score 8 or greater.

Materials and Methods: We identified 159 patients who underwent prostatectomy without neoadjuvant therapy for biopsy proven Gleason score 8 or greater T1c-T2N0M0 cancer between 1996 and 2006. Univariate and multivariate analyses were performed to predict extraprostatic extension using side specific data, including clinical features and biopsy findings.

Results: Organ confined cancer was pathologically confirmed in 84 of 159 patients (52.8%). Side specific analysis was practicable on 124 sides (124 men) and side specific extraprostatic extension was found on 48 of the 124 sides (38.7%). Gleason grade 5 element, maximum tumor length, percent of positive cores, positive basal cores and side specific palpable disease were significantly associated with side specific extraprostatic extension. On multivariate analysis maximum tumor length and a positive basal core were independent predictors of side specific extraprostatic extension ($p < 0.001$ and 0.033, respectively). When maximum tumor length was less than 7 mm and the basal core was negative for cancer, the incidence of side specific extraprostatic extension was low (2 of 35 cases or 5.7%). In contrast, the risk of side specific extraprostatic extension was 56.8% (25 of 44 cases) when maximum tumor length was 7 mm or greater and the basal core was positive for cancer.

Conclusions: Applying our criteria for prostatectomy could significantly decrease the risk of inadequate cancer control and increase the probability of maintaining potency in patients with prostate cancer with biopsy Gleason score 8 or greater.

Key Words: prostate, prostatic neoplasms, erectile dysfunction, neoplasm invasiveness, prostatectomy

Historically patients with high grade prostate cancer (GS 8 or greater in biopsy) were not considered good candidates for radical prostatectomy because of the association with a high incidence of EPE and metastasis, and poor survival rates.[1,2] However, the widespread use of the PSA assay has resulted in the detection of prostate cancers at an early stage, which is potentially curable by surgery.[3] In 2004 we reported long-term disease-free survival after prostatectomy as monotherapy in men with high grade prostate cancer.[4] Although only 58 of the 188 patients (30.9%) assigned a GS of 8 or greater disease in the prostatectomy specimen had cancer confined to the prostate (pT2), 108 (57.4%) had specimen confined disease. Furthermore, 128 of the 188 patients (68.1%) had no evidence of prostate cancer recurrence at a median followup of 60 months. These findings suggest that high grade prostate cancer is potentially curable by prostatectomy alone if we can select patients properly.

Prostate cancer EPE is an important finding because of its implications regarding tumor biology, positive surgical margins, and disease-free and disease specific survival.[4–10] The decreased incidence of EPE provides an opportunity to maximize complete cancer resection and minimize the morbidity associated with radical prostatectomy even in men who have high grade cancer in biopsy specimens.[4,11–15] Several established criteria and nomograms show the probability of EPE using preoperative variables, such as clinical stage, PSA value and biopsy features.[5–9] We also previously reported criteria that predict prostate cancer side specific EPE.[10] On our multivariate analysis GS was not a significant predictor of EPE and, therefore, it was not included in our previous model. Nevertheless, we remained reluctant to perform nerve sparing prostatectomy in patients with biopsy GS 8 or greater because we previously reported a 69.1% incidence of EPE in patients with GS 8 or greater disease in the prostatectomy specimens.[4] Many surgeons are also hesitant to consider men with GS 8 or greater disease as candidates for nerve sparing surgery because the surgical boundaries are obviously reduced with this procedure. However, persistent trends in prostate cancer stage migration prompted reconsideration of this position and the development of criteria to select patients with biopsy GS 8 or greater disease who might benefit from nerve sparing prostatectomy.

There are few reports of the likelihood of EPE in men with biopsy GS 8 or greater disease. We assessed the ability

Submitted for publication March 17, 2008.

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† Financial interest and/or other relationship with Endocare and Gen-Probe.

DOI:10.1016/j.juro.2008.08.023

of preoperative clinical and pathological variables to predict side specific EPE in men with biopsy GS 8 or greater disease.

MATERIALS AND METHODS

Patients and Data Extraction

Between January 1996 and December 2006 we identified 159 patients who underwent prostatectomy for biopsy GS 8 or greater, clinical T1c-T2N0M0 cancer. None of the men had received neoadjuvant therapy. In this study we focused on men with biopsy GS 8 or greater because prostatectomy GS cannot be used preoperatively. Previous studies have shown that biopsy features such as positive basal core location and the proportion of positive biopsy cores are significant predictors of EPE.[5–10] Therefore, 35 patients were excluded from further analysis because their biopsy samples were labeled right and left without information on the specific location. We evaluated 124 patients with adequate documentation of biopsy features, including the core location and tumor length of each core, to optimize analysis for side specific EPE. We analyzed only sides with biopsy confirmed GS 8 or greater in our model. Adequate documentation of biopsy features involving the core location, tumor length of each core and GS 8 or greater disease was available on a total of 124 sides in the 124 evaluable men.

Side specific biopsy features (Gleason grade 5 component, maximum tumor length in cores, proportion of positive cores, positive basal core and proportion of the tumor length with GS 8 or greater) and clinical features (patient age, PSA, prostate volume, PSA density and side specific palpable disease) were correlated with the finding of side specific EPE. Because of an imbalance in the number of patients, we excluded ethnicity as a variable on univariate and multivariate analysis.

Pathological Findings

All results of diagnostic biopsies performed elsewhere were reviewed and reevaluated by pathologists at our institution. The final diagnoses on biopsy were obtained from pathology reports at our institution.

Radical prostatectomy specimens were submitted for histological examination by a single pathologist (PT), as described previously.[16] Briefly, each specimen was weighed, measured, inked and fixed in 10% formalin. After fixation the apical portion was separated from the rest of the prostate and sectioned radially. The remaining prostate was sectioned at 4 mm intervals in a transverse plane perpendicular to the posterior surface. The margin at the base of the prostate was evaluated with perpendicular sections. Cross-sections were divided and submitted in standard cassettes.

Each tumor focus in a prostatectomy specimen was graded according to the Gleason grading system. The assigned histological grade was that of the dominant tumor focus except for dominant transition zone tumors of lower grade, which were assigned the Gleason grade from the peripheral zone focus with the highest Gleason grade.

Based on pathological examination tumors were classified into a pT category including organ confined tumor with a negative surgical margin—pT2-, positive surgical margin without evidence of extracapsular extension—pT2+, EPE with and without positive surgical margins—pT3a− and pT3a+, respectively, and seminal vesicle invasion with or without positive surgical margins—pT3b− and pT3b+, respectively.

EPE was defined as tumor in periprostatic adipose tissue. A positive resection margin was defined as tumor in contact with ink on the surface of the specimen. In accordance with the purpose of the study tumor invasion in the intraprostatic and extraprostatic portion of the seminal vesicle were excluded from the determination of EPE.

EPE sites were noted and reported by side as the NVB, PL, base, apex, anterior, posterior and lateral regions. The NVB and PL regions were grouped together as the NVB/PL region since EPE at either of these locations potentially increases the risk of a positive margin if the NVB is spared.[9,10] All prostatectomy results relating to EPE were reevaluated by side.

Statistics

The continuous variables assessed were maximum tumor length in mm, percent of positive cores, percent of GS 8 or greater component, patient age in years, PSA in ng/ml, prostate volume in cc and PSA density in ng/ml/cc. The categorical variables assessed were side specific clinical stage (T1c or T2), presence of a Gleason grade 5 component and tumor location (positive or negative basal cores). The significance of associations between side specific EPE and variables were analyzed using the Mann-Whitney U test. Pearson's correlation coefficient was used to estimate the degree of correlation between variables. Forward stepwise multivariate logistic regression analysis was done to determine the independent association of variables with side specific EPE. All analyses were performed using SPSS®, version 12.0 with $p < 0.05$ considered statistically significant. The AUC from ROC curve analysis was used to confirm predictive accuracy and determine the cutoff values of significant continuous variables for predicting side specific EPE.

RESULTS

Table 1 lists patient characteristics. Table 2 shows the pathological results of prostatectomy specimens. Of 159 patients 89 (56.0%) had GS 8 or greater tumors in prostatectomy specimens, while 70 (44.0%) showed downgrading to

TABLE 1. *Patient and disease characteristics*

Characteristics		
No. Pts	159	
Median age (range)	63	(41–74)
No. ethnicity (%):		
White	130	(81.8)
Black	14	(8.8)
Hispanic	12	(7.5)
Asian	3	(1.9)
Median ng/ml PSA (range)	6.3	(0.7–46.6)
Median cc TRUS prostate vol (range)	34.2	(12.3–106.2)
Median ng/ml/cc PSA density (range)	0.180	(0.02–1.879)
No. clinical stage (%):		
T1c	54	(34.0)
T2	105	(66.0)
No. biopsy scheme (%):		
Bilat (rt vs lt)	35	(22.0)
Sextant	59	(37.1)
Extended	65	(40.9)
No. biopsy GS:		
8	129	(81.1)
9	28	(17.6)
10	2	(1.3)