156 UNIFOCAL AND MULTIFOCAL PROSTATE CANCER: A COMPARISON OF CLINICOPATHOLOGIC FEATURES

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INTRODUCTION AND OBJECTIVE: Early detection, stage migration, and emphasis on health related quality of life has led to increasing interest in focal therapy for prostate cancer (PCa). Advocates attempt to map prostate tumors in order to limit their patient population to those with unifocal disease. Unfortunately, no descriptive studies evaluating single focus prostate cancer have been performed and little is known regarding the unique biology of this disease. The objective of this study is to characterize the clinico-pathologic behavior of unifocal PCa in comparison to its multifocal counterpart.

METHODS: The Center for Prostate Disease Research (CPDR) database was queried for all prostatectomy specimens obtained from 1994 to 2004. All specimens were analyzed at the Armed Forces Institute of Pathology utilizing whole mount and 2 mm step sectioning. Tumors were comprehensively mapped to include number of tumor foci and calculation of total tumor volume. Patients with single focus PCa were compared to those demonstrating multifocal disease. Primary outcomes were pathologic stage and biochemical recurrence, while secondary outcomes were Gleason sum and total tumor volume. A p-value of <0.05 was considered statistically significant using the chi-square, Fisher exact, and Student’s T-test.

RESULTS: A total of 1012 prostatectomies were examined with 109 (10.7%) demonstrating a single focus of PCa. Median patient age was 60 in the unifocal and 61 in the multifocal cohorts. Median PSA was 10 for the unifocal and 7.4 for the multifocal cohorts. Median total tumor volume was 5.2 cc for unifocal and 4.2 cc for multifocal disease. The unifocal cohort Gleason sums were 2-6 in 51%, 7 in 31.6%, and 8-10 in 17.3%. The multifocal cohort Gleason sums were 2-6 in 56.8%, 7 in 29.9%, and 8-10 in 10.1%. Extraprostatic extension was noted in 56.0% of cases with unifocal and 36.1% of cases with multifocal disease. In total, 27% of unifocal and 15.5% of multifocal disease had biochemical recurrence. Of the patients with organ confined (pT2) disease, 6.4% of unifocal and 5.2% of multifocal disease had a PSA recurrence. The frequency of single focus CaP stratified by year of surgery was: 1993-1996 (17%), 1997-2000 (9.4%), 2001-2004 (8.6%).

CONCLUSIONS: Unifocal prostate cancer is a more aggressive entity than its multifocal counterpart. PSA, Gleason sum, total tumor volume, extracapsular disease, and biochemical recurrence were significantly higher in the unifocal population. With intensive prostate cancer screening the incidence of single focus prostate cancer has decreased.

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157 DOES PATHOLOGICAL GLEASON SCORE RE-REVIEW BY A MODERN PATHOLOGIST IMPROVE RISK STRATIFICATION RELATIVE TO HISTORICAL GLEASON SCORE?

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INTRODUCTION AND OBJECTIVE: Clinicians have long used Gleason scores to assess the prognosis of men with prostate cancer. In recent years, there have been trends toward fewer low Gleason scores and a general bunching of Gleason scores between 6 and 8. Possible reasons are fewer low-grade cancers found by TURP but also likely reflect changes in pathological interpretation. Whether these changes in Gleason grading have overall improved, worsened, or had no effect on the usefulness of Gleason score for risk stratification is unclear. We sought to assess the utility of Gleason grade to predict PSA recurrence after radical prostatectomy (RP) using the historically graded Gleason score at the time of surgery versus a grade given by a contemporary pathologist in 2008.

METHODS: Men treated with RP from either the Duke Prostate Center (DPC; n: 195) and the Durham VA Medical Center (DVAMC; n: 65) were selected to have their original biopsy (DVAMC only) and prostatectomy slides (DVAMC and DPC) reviewed by one of three pathologists. Inclusion criteria were RP between 1993 and 1997 and no receipt of any neoadjuvant or adjuvant therapy prior to PSA recurrence. Historical and contemporary Gleason scores were categorized into the following groups: 2-6, 7, and 8-10. The ability of categorized Gleason score to predict PSA recurrence was assessed using the concordance index C, and were compared to assess the predictive accuracy of historic vs. contemporary Gleason.

RESULTS: In DVAMC, historical biopsy Gleason scores (index C = 0.66) predicted disease-free survival with greater accuracy than contemporary biopsy Gleason scores (index C=0.63). Historical prostatectomy Gleason scores outperformed contemporary prostatectomy scores in predicting disease-free survival in both DVAMC (0.66 vs. 0.64) and DPC (0.67 vs. 0.63) study populations.

CONCLUSIONS: Historical Gleason scores had higher predictive accuracy when compared to contemporary scoring of both prostate biopsy and prostatectomy specimens in predicting disease-free survival. This suggests that historical Gleason scoring may be a better predictor of biochemical recurrence. Further study in larger and different patient populations is needed to confirm these findings. If validated, these findings suggest Gleason score as assigned by contemporary pathologists may provide less risk stratification than in the past arguing that new and better markers of progression are needed.

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158 INTEROBSERVER VARIABILITY IN HISTOLOGIC EVALUATION OF RADICAL PROSTATECTOMY (RP) SPECIMENS BETWEEN CENTRAL AND LOCAL PATHOLOGISTS: FINDINGS OF A MULTINATIONAL CLINICAL TRIAL

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INTRODUCTION AND OBJECTIVE: TAX 3501 is a randomized phase III multinational trial comparing treatment with docetaxel plus androgen-deprivation therapy with androgen deprivation alone after RP in high-risk patients with prostate cancer. Eligible patients had a predicted 5-year progression-free survival of ≥60% by Kattan’s nomogram based on central pathologist (CP) review. The current analysis compared the histologic evaluation of RP specimens by local pathologists (LP) and CP.

METHODS: All RP sections were blindly re-reviewed by one of two urologic CP on the trial. Data on Gleason Score (GS), organ confined vs focal vs extensive extraprostatic extension (OC vs FEPE vs EEPE), margin (MG), seminal vesicle (SV) and lymph node (LN) status were compared in samples from 257 consecutive RP patients.

RESULTS: GS: agreed in 181/257 (70%) of RP. Among 76 cases (30%) with GSc variance, CP review upgraded 57 (75%) and downgraded 19 (25%). Most frequent GSc upgrades were from 7 to 8/9 and most frequent downgrades were from 8 to 7. Upgrades in 37% and 2% of cases were by 2 and 3 GSc increments, respectively; 21% of downgrades were by 2 GSc increments; all remaining changes in GSc were by 1.

OC/FEPE/EEPE: agreed in 179/256 (70%) of RP. Among 77 cases (30%) with stage variance, CP upstaged 70 (91%) and downstaged 7 (9%). Most frequent upstaging was from FEPE to EEPE (44%) and from OC to EEPE (27%). LP staged 25% of RP as capsular invasion, which were restaged as EEPE. Reasons leading to understaging EEPE included ambiguity at apex, tumor with desmoplasia lacking surrounding fat, ambiguity in definition of capsular invasion.

SV Status: agreed in 238/257 (93%) of RP. Among 19 cases (7%) with SV variance, an almost equal number of under/overcalling was done by LP compared to CP. Overcalling was due to presence of tumor in peri-SV tissue (not in muscle), ejaculatory duct, and prostate tissue adjacent to SV.

MG Status: agreed in 229/256 (89%) of RP. Among 27 cases (11%) with MG variance, CP review led to reclassification from (-) to (+) in 17 (62%)