Prostate Total Tumor Extent Versus Index Tumor Extent—Which is Predictive of Biochemical Recurrence Following Radical Prostatectomy?

Athanase Billis,* Luciana R. Meirelles, Leandro L. L. Freitas, Aline S. Polidoro, Hamilton A. Fernandes, Mariana M. Padilha, Luis A. Magna and Ubirajara Ferreira

From the Departments of Pathology (AB, LRM, LLLF, ASP, HAF, MMP), Medical Genetics/Biostatistics (LAM) and Urology (UF), School of Medicine, University of Campinas, São Paulo, Brazil

Purpose: It is controversial whether tumor extent in radical prostatectomies predicts biochemical recurrence following surgery. We compared the predictive value of total tumor extent vs dominant nodule (index tumor) extent.

Materials and Methods: A mean of 32 paraffin blocks was processed from prostate surgical specimens step sectioned at 3 to 5 mm intervals from 300 patients treated with radical retropubic prostatectomy. Each transverse section was subdivided into 2 anterolateral and 2 posterolateral quadrants. Tumor extent was evaluated by a semiquantitative point count method. Dominant nodule extent was recorded as the maximal number of positive points of the largest single focus of cancer in the quadrants. Time to biochemical recurrence was analyzed by Kaplan-Meier product limit analysis. Prediction of shorter time to biochemical recurrence was determined by univariate and multivariate Cox proportional hazards models.

Results: Except for age and race, total and index tumor extent was significantly associated with higher preoperative prostate specific antigen, clinical stage T2, pathological stage greater than T2, positive surgical margins and higher radical prostatectomy Gleason score. Total and index tumor extent was significantly associated with time to biochemical recurrence in Kaplan-Meier estimates. Total and index tumor extent significantly predicted shorter time to biochemical recurrence on univariate analysis but only index tumor extent was an independent predictor of time to biochemical recurrence on multivariate analysis.

Conclusions: The study indicates that any tumor extent estimate in surgical specimens should be related to the dominant nodule (index tumor) and not to total tumor extent.

Key Words: prostate; prostatic neoplasms; prostatectomy; prostate-specific antigen; pathology, surgical

Abbreviations and Acronyms

BCR = biochemical recurrence
PSA = prostate specific antigen
PSM = positive surgical margin
RP = radical prostatectomy
TBCR = time to BCR

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* Correspondence: Department of Pathology, School of Medicine, University of Campinas (Unicamp), Rua Tessália Vieira de Camargo, 126, CEP 13083-887 Campinas, São Paulo, Brazil (FAX: +55 19 3289-38-97; e-mail: athanase@fcm.unicamp.br).

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THERE is no controversy that prostate tumor extent on needle biopsy should be reported.[1–4] The only controversy is related to which method of tumor quantification should be adopted.[3,5–7] However, it is controversial whether tumor extent on RP specimens is an independent prognostic factor of BCR following surgery.[8]

Because prostate cancer grows irregularly, volume measurement is technically much more difficult than in other organs. The most accurate method is to use computer assisted image analysis systems, which is not feasible for routine clinical practice. Other alternative, simpler methods have been proposed, including the diameter of the largest

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tumor focus, the number of tumor foci, the number or percent of involved blocks, a grid with 3.0 mm squares, the semiquantitative point count method and even eye examination of the glass slides.[9–16]

Several groups reported that tumor extent on RP is an independent predictor of disease recurrence.[14–16] However, others were unfavorable, arguing that tumor extent does not provide additional information beyond that of Gleason score and surgical margin status.[17–19] Alternatively, in other studies the extent of the dominant nodule (index tumor) was an independent risk factor for PSA recurrence after RP.[13,20,21]

We compared total tumor extent vs dominant nodule (index tumor) extent as independent predictors of BCR following RP.

MATERIALS AND METHODS

This retrospective study was based on 300 consecutive patients with clinical stage T1c (144) and T2 (156) treated with retropubic RP by 1 surgeon (UF). Several clinicopathological variables were studied.

After RP serum PSA was measured every 3 months during year 1, every 6 months during year 2 and annually thereafter. No patient in this series received radiotherapy or androgen manipulation before or after surgery. Total serum PSA was measured using the previously validated Immulite® PSA kit. Postoperative BCR was considered PSA 0.2 ng/ml or greater according to the American Urological Association recommendation.[22] Patients without evidence of BCR were censored at last followup. The study was approved by our institutional committee of ethics.

Surgical specimens were step sectioned at 3 to 5 mm intervals and embedded in paraffin. A mean of 32 paraffin blocks was processed. Sections (6 μm) of each block were stained with hematoxylin and eosin. Each transverse section of the prostate was subdivided into 2 anterolateral and 2 posterolateral quadrants. Using the cone method 8 sections from the bladder neck and 8 from the apex were obtained.

PSM was defined as cancer cells in contact with the inked specimen surface. Extraprostatic extension was diagnosed when cancer was seen in adipose tissue, and in case of a desmoplastic response when a protuberance corresponding to tumor extension into periprostatic tissue was seen. Seminal vesicle invasion occurred when there was involvement of the muscular coat.

Tumor extent at RP was evaluated by a previously described semiquantitative point count method.[9] Briefly, each quadrant of the transverse sections was drawn on paper and contained 8 equidistant points. During microscopic examination of the slides, the tumor area was drawn on the correspondent quadrant on the paper. At the end of examination the number of positive points represented an estimate of tumor extent.

Figure 1 shows the drawing included in the pathology report with 8 equidistant points per quadrant. Total tumor extent was recorded as the total sum of the positive points of all transverse quadrants. Index tumor extent (dominant nodule) was recorded as the maximum number of positive points for the largest single focus of cancer in the quadrants. Total and index tumor extent was recorded as 28 and as 7 positive points, respectively (fig. 1). All cases were reviewed by a senior uropathologist (AB).

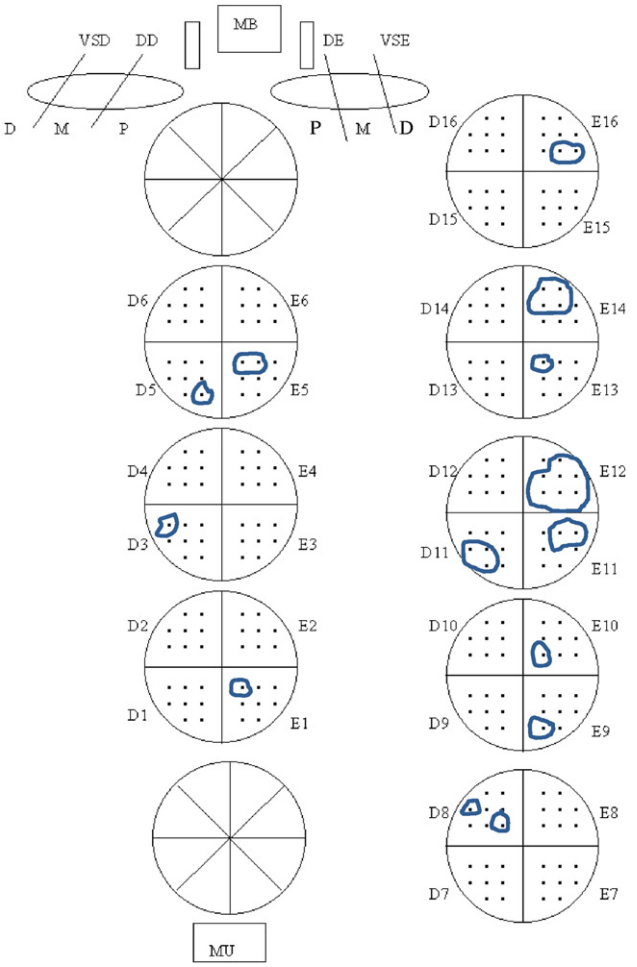

Figure 1. Semiquantitative point count method to evaluate tumor extent. In this case total tumor extent was recorded as 28 positive points. Quadrant E12 shows largest single cancer focus or dominant nodule of all quadrants, recorded as 7 index tumor positive points.

Statistical Analysis

Data were analyzed using the Fisher exact test to compare proportions, the Mann-Whitney test to compare means and Kaplan-Meier product limit analysis for TBCR using the log rank test for comparison between the groups according to the median value of positive points, including 26 for total tumor extent evaluation and 4 for index tumor extent evaluation. Univariate and multivariate Cox stepwise logistic regression models were used to identify significant predictors of shorter TBCR. Statistical significance was considered at $p < 0.05$. All statistical analyses were performed using PASW® Statistics 18.0.

RESULTS

Clinicopathological Findings

Except for age and race, total and index tumor extent was significantly associated with higher preop-