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Original article

Comparison of prostate cancer tumor volume and percent cancer in prediction of biochemical recurrence and cancer specific survival☆,☆☆

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Abstract

Objectives: Tumor volume and percent cancer (ratio of tumor volume/prostate volume) have been proposed as predictors of biochemical recurrence and cancer specific survival after radical prostatectomy. However, their relative merits as prognosticators have not been tested. We therefore evaluated and compared tumor volume and percent cancer as independent predictors of biochemical recurrence and prostate cancer specific death after radical prostatectomy.

Methods and Materials: A retrospective review of 739 patients who underwent radical prostatectomy for prostate cancer between 1984 and 2004 was conducted. Median follow-up was 91.7 months, and 22 patients died of prostate cancer. Univariate and multivariate analysis evaluated the following factors in predicting biochemical recurrence and prostate cancer specific death: tumor volume, prostate volume, percent cancer, Gleason score, percentage of Gleason grade 4/5, margin status, capsular invasion status, seminal vesicle invasion status, preoperative PSA, and lymph node status.

Results: In univariate analysis, both tumor volume ($P < 0.001$) and percent cancer ($P < 0.001$) significantly correlated with biochemical recurrence. Since they are highly correlated, they did not predict outcome independently when included in the same model; however, both were highly predictive for biochemical recurrence in separate multivariate models ($P = 0.01$ for both). Both also correlated with cancer specific survival as single variables; however, in separate multivariate models, only tumor volume ($P = 0.03$) predicted death, while percent cancer did not ($P = 0.09$).

Conclusions: Tumor volume and percent cancer are independent predictors of recurrence after radical prostatectomy. However, in our series, tumor volume predicted cancer specific death better than percent cancer. Therefore, accurate determination of tumor volume, along with other accepted pathologic indices, is sufficient and preferred over percent cancer for prognostication after radical prostatectomy.

Keywords: Prostate cancer; Radical prostatectomy; Tumor volume; Biochemical recurrence; Cancer specific survival

1. Introduction

After radical prostatectomy, clinicians utilize pathologic data to determine the risk of biochemical recurrence, progression, and cancer specific survival. Traditionally, those indices have included Gleason score, surgical margin positivity, and pathologic stage, including the presence of capsular invasion, seminal vesicle involvement, and lymph node metastases. Several investigators have suggested that tumor volume and percent cancer (cancer volume/prostate volume or cancer index) are independent predictors of recurrence [1–6]. However, there is no agreement on the best methods for assessing tumor volume or percent cancer [7]. As a result, studies assessing tumor volume and percent cancer as independent predictors of biochemical recurrence and cancer specific survival have produced conflicting results, leading some investigators to doubt their utility [8,9]. Furthermore, no study has compared systematically the relative merits of tumor volume and percent cancer. While

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these two variables are highly related, since percent cancer depends on estimates of tumor volume, they are not identical. Tumors with identical volumes can have large differences in percent cancer due to the large variation in prostate sizes that are encountered clinically. Therefore, we examined whether tumor volume and percent cancer predicted biochemical recurrence and cancer specific survival after radical prostatectomy.

2. Materials and methods

The patient cohort included 739 men who underwent radical retropubic prostatectomy at Stanford University Medical Center for clinically localized prostate cancer between 1984 and 2004 by multiple surgeons. None of these patients had undergone preoperative or adjuvant therapy of any type. All patients signed an IRB approved consent for use of their clinical and pathologic data. Fresh specimens were weighed and fresh weight was used as a surrogate for total prostate volume. The specimens were then fixed in formalin and serially sectioned at 3 mm intervals in a plane perpendicular to the rectal surface and embedded in paraffin. Specimens were then cut at 5 um and examined microscopically. Between 1984 and 2002, all prostate cancer on each individual slide was traced manually. Tumor volume of the largest incident tumor was then calculated utilizing a software program developed by our Department of Pathology as described previously [10]. The individual slides were also examined by a single pathologist for the presence of standard pathologic indices, including pathologic stage, margin positivity, Gleason score, percentage Gleason pattern 4/5, and lymph node involvement, seminal vesicle involvement, and extracapsular extension of tumor. Clinical parameters were examined for significance in predicting for biochemical recurrence, progression, and prostate cancer-specific survival. These included tumor volume, prostate volume, percent cancer (tumor volume/prostate volume), Gleason score, percent Gleason 4/5, surgical margin status, capsular invasion, seminal vesicle involvement, preoperative PSA, and lymph node status.

Patient follow-up included serum PSA measurements at every 3 months for 1 year, every 6 months for the following year, and annually thereafter, provided there was no evidence of biochemical recurrence. Biochemical failure was defined by a serum PSA >0.07 ng/ml and rising on subsequent determinations. Those patients who received their follow-up elsewhere were contacted directly and copies of their PSA results were sent to our institution. Review of death certificates, direct contact of the patients' families, or review of the medical record confirmed prostate cancer specific death in 22 patients.

The association between tumor volume and percent cancer was tested by Pearson correlation. Univariate and multivariate Cox proportional hazards models were used to evaluate the relationships between the clinical and pathologic variables and disease recurrence or prostate cancer death. Statistical tests were all two-sided. All statistical analyses were carried out in R package, version 2.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

Table 1
Patient data

Variable	Median value (25% CI–75% CI) or % of cohort
Age (years)	63.4 (58.4–67.8)
PSA (ng/ml)	7.4 (4.9–11.3)
Tumor volume (cc)	2.4 (1.23–4.92)
Prostate volume (g)	45.0 (37.7–59.0)
Percent cancer (%)	5.6 (2.7–11.3)
Recurrence (no. patients)	198 (26.7%)
Time to recurrence (months)	69.8 (43.3–102)
Prostate cancer specific Death (no. patients)	22 (3%)
Time to death (months)	110 (27.9–201.6)
Follow up (months)	91.7 (63.8–124)
Gleason score 3+3	160 (21.7%)
Gleason score 3+4	412 (55.8%)
Gleason score 3+5	1 (0.1%)
Gleason score 4+3	159 (21.5%)
Gleason score 4+4	3 (0.4%)
Gleason score 4+5	4 (0.5%)

Table 2
Biochemical recurrence univariate analysis

	OR (95% CI)	*P* value
Tumor volume	1.02 (1.005–1.04)	<0.001
Prostate volume	0.99 (0.98–1.00)	0.2
Percent cancer	1.03 (1.03–1.04)	<0.001
% 4/5	1.03 (1.02–1.03)	<0.001
PSA	1.04 (1.03–1.05)	<0.001
Positive margin	4.12 (3.1–5.47)	<0.001
Capsular invasion	6.07 (4.51–8.16)	<0.001
Seminal vesicle	7.77 (5.65–10.7)	<0.001
Lymph node	8.62 (5.96–12.5)	<0.001
Gleason 3+3	0.07	<0.001
Gleason 3+4	1.0	Reference value
Gleason 4+3	2.85	<0.001
Gleason ≥ 4+4	4.73	<0.001

3. Results

Data on patient age, preoperative PSA, and pathologic features are summarized in Table 1. Like many series, the most common tumor grades were Gleason 3+3, 3+4, and 4+3. The median follow-up was 91.7 months (interquartile range 63.8–124 months), and 22 patients (3%) died of prostate cancer at a median of 110 months (interquartile range 27.9–201.6). There were no operative deaths.