Prostogram Predicted Brachytherapy Outcomes are Not Universally Accurate: An Analysis Based on the M. D. Anderson Cancer Center Experience With ^{125}Iodine Brachytherapy

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Abbreviations and Acronyms

AJCC = American Joint Committee on Cancer

ASTRO = American Society for Therapeutic Radiology and Oncology

C = concordance

PSA = prostate specific antigen

Submitted for publication August 8, 2008.

Study received M. D. Anderson Cancer Center institutional review board approval.

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† Financial interest and/or other relationship with Calypso Medical and Amgen.

Purpose: Many clinicians use Prostogram data to advise patients selecting prostate cancer therapy. We examined whether the Prostogram accurately predicted recurrence at 5 years in patients treated with ^{125}I brachytherapy at 1 tertiary cancer center.

Materials and Methods: We retrospectively reviewed the records of 208 consecutive patients with prostate cancer treated with a permanent ^{125}I implant without neoadjuvant androgen deprivation therapy at 1 tertiary cancer center during 1998 to 2006. In each patient the Prostogram brachytherapy formula was used to calculate 5-year biochemical recurrence-free survival probability based on clinical stage, Gleason sum score, prostate specific antigen and the receipt or not of external beam radiotherapy. Recurrence was defined as clinical relapse, death from disease, posttreatment androgen deprivation therapy, secondary treatments administered before prostate specific antigen failure or biochemical recurrence based on the Kattan modification of the American Society for Therapeutic Radiology and Oncology definition of biochemical recurrence after external beam radiation therapy. Patients were divided into quartiles based on Prostogram predicted 5-year recurrence-free survival probability and mean probability was compared to the actual 5-year recurrence-free survival rate in each quartile. Harrell's concordance statistic was used to assess the predictive accuracy of the nomogram.

Results: Actual 5-year biochemical recurrence-free survival rates were superior to Prostogram predicted probabilities, including 89% vs 80%, 87% vs 86%, 100% vs 89% and 100% vs 94% in quartiles 1 to 4, respectively. Harrell's concordance value was 0.487 (95% CI 0.369–0.605), indicating that the predictive accuracy of the nomogram in our patients was less than 50%.

Conclusions: The Prostogram did not predict recurrence after permanent prostate brachytherapy in this series. Institutional variability requires that clinicians be cautious when using the Prostogram to counsel patients about the probability of success after permanent prostate brachytherapy.

Key Words: prostate, brachytherapy, prostatic neoplasms, nomograms, mortality

In men with prostate cancer multiple potentially curative standard of care treatment options are available, including radical prostatectomy, external beam radiotherapy and brachytherapy. Choosing which treatment to

0022-5347/09/1814-1658/0
THE JOURNAL OF UROLOGY®

Vol. 181, 1658-1664, April 2009
Printed in U.S.A.
DOI:10.1016/j.juro.2008.11.101

pursue can be difficult. Recently in an effort to provide patients and clinicians with information that can guide the decision making process nomograms have been developed that indicate the predicted outcomes of different treatments in an individual. These nomograms can be downloaded free of charge from the Internet and incorporated into daily clinical practice.[1] One such nomogram, the Prostogram, predicts worse 5-year recurrence-free survival rates for brachytherapy than for radical prostatectomy or external beam radiotherapy in men presenting with low risk features, such as PSA 8 ng/ml, a Gleason score of 6 (3 + 3) in 1 of 12 cores and clinical T1c disease.[2]

At the University of Texas M. D. Anderson Cancer Center it has been our experience that brachytherapy outcomes are excellent. Under an institutional review board approved protocol we recently evaluated data on 330 patients treated with prostate brachytherapy at M. D. Anderson Cancer Center since the implant program at the institution began in 1998. At a median followup of 61 months we found a 5-year biochemical recurrence-free survival rate of 96.4%,[3] which compares favorably with rates in men treated with radical prostatectomy or external beam radiotherapy.

We determined whether the Prostogram is generalizable to patients undergoing ^{125}I brachytherapy at M. D. Anderson Cancer Center by comparing Prostogram predicted outcomes with actual clinical outcomes in such patients.

MATERIALS AND METHODS

The M. D. Anderson Cancer Center institutional review board approved this study and waived the requirement for informed consent. The medical records of all 339 patients with prostate cancer treated with a permanent ^{125}I implant at M. D. Anderson Cancer Center from 1998 through 2006 were retrospectively reviewed. Because the Prostogram does not apply to patients treated with neoadjuvant androgen deprivation therapy, we excluded the 128 who received such therapy. An additional 3 patients were excluded based on stage criteria or lack of PSA followup, leaving 208 available for analysis.

Recurrence was defined as clinical relapse, death from disease, secondary treatments administered before PSA failure, any posttreatment administration of androgen deprivation therapy or biochemical recurrence according to the Kattan modification of the ASTRO definition of biochemical recurrence after external beam radiation therapy. In other words patients with a total of 3 PSA increases (with or without stable intervening PSA levels) and no PSA decreases were considered to have biochemical recurrence. In those with a PSA increase but no biochemical recurrence at last followup the followup was truncated at the PSA measurement immediately before the first increase.

In each patient Prostogram code (SAS®, version 9.1.3) was used to calculate the 5-year biochemical recurrence-free survival probability based on pretreatment PSA, Gleason score, clinical tumor classification according to the AJCC staging system, 5th edition and whether the patient had received external beam radiation therapy, in addition to brachytherapy.

Concordance between the predicted probabilities of biochemical recurrence-free survival and the actual recurrence experience of eligible patients was assessed using Harrell's C based on the Kattan recurrence criterion, which was calculated with the function rcorr.cens from the Hmisc library[4] in the R statistical software package, version 2.6.1. This is the same statistical tool that was used to evaluate the original Prostogram.[1]

Patients were then divided into quartiles based on the Prostogram predicted 5-year survival probability. In each patient with biochemical recurrence according to the Kattan modification the clinical course was examined. If such a patient had a PSA increase followed by a subsequent decrease in PSA without any intervention (a PSA bounce), had received no salvage therapy and had no evidence of disease at the time of analysis, the patient was considered free of biochemical recurrence. For each quartile the mean of Prostogram predicted, 5-year biochemical recurrence-free survival probabilities was compared to the actual 5-year biochemical recurrence-free survival rate. The calibration of actual and predicted 5-year freedom from recurrence was assessed by graphs of these measures. Simple linear regression was used to fit lines relating actual 5-year freedom from recurrence to predicted 5-year freedom from recurrence.

RESULTS

Patient Characteristics

The table lists patient characteristics. Median maximum followup in censored patients was 38 months. Median pretreatment PSA in all 208 patients was 5.6 ng/ml. Of the patients 82% and 17% presented with a Gleason score of 6 and 7, while 74% and 25% presented with T1c and T2a disease, respectively. Of the patients 97% were treated with brachytherapy alone without external beam radiotherapy.

Concordance Between Predicted and Actual Outcomes

Harrell's C value for Prostogram predicted and actual 5-year biochemical recurrence-free survival was 0.487 (95% CI 0.369–0.605), indicating that the predictive accuracy of the Prostogram was less than 50%.

Predicted vs Actual Outcomes by Quartile

Actual rates of freedom from recurrence were superior to Prostogram predicted probabilities in each quartile, including 89% vs 80%, 87% vs 86%, 100% vs 89% and 100% vs 94% in quartiles 1 to 4, respectively (fig. 1). Of the 15 patients classified by the