Nomogram Predicting the Probability of Early Recurrence After Radical Prostatectomy for Prostate Cancer

Jochen Walz,*,† Felix K.-H. Chun, Eric A. Klein, Alwyn Reuther, Fred Saad, Markus Graefen, Hartwig Huland and Pierre I. Karakiewicz‡

From the Cancer Prognostics and Health Outcomes Unit (JW, PIK), and Department of Urology (FS, PIK), University of Montreal, Montreal, Canada, Department of Urology, Institut Paoli-Calmettes, Marseille, France (JW), Department of Urology (FKC, HH) and Martini Clinic–Prostate Cancer Center (MG, HH), University Medical Centre Eppendorf, Hamburg, Germany, and Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, Ohio (EAK, AR)

Purpose: We developed a nomogram predicting the probability of early biochemical recurrence after radical prostatectomy because early recurrence predisposes to distant metastasis and prostate cancer related mortality. Identifying patients at risk for early recurrence may improve prognosis as early institution of adjuvant therapy may reduce the risk of progression.

Materials and Methods: From January 1992 to December 2005, 2,911 patients underwent radical prostatectomy for localized prostate cancer. Cox regression models addressing biochemical recurrence after radical prostatectomy were used to identify significant predictors. Age, prostate specific antigen, pathological Gleason sum, surgical margin, extracapsular extension, seminal vesicle invasion and lymph node invasion were considered. A nomogram predicting the probability of biochemical recurrence-free survival within 2 years after radical prostatectomy was developed. Data from an independent center were used for external validation (2,875).

Results: In both cohorts combined during the first 2 years 11.0% (639) of all patients experienced relapse which accounted for 58.5% of all observed biochemical recurrence. In the development cohort except for age all covariates represented significant predictors of biochemical recurrence after radical prostatectomy. Pathological Gleason sum 7 or greater, seminal vesicle invasion and lymph node invasion were the most powerful predictors of biochemical recurrence. The accuracy (c-index) of the nomogram predicting biochemical recurrence-free survival within 2 years after radical prostatectomy was 0.82 in the external validation cohort.

Conclusions: Two-thirds of all instances of relapse occur during the first 2 years after radical prostatectomy. Those patients can be highly accurately identified with our nomogram. They might benefit the most from adjuvant treatment and could be the ideal candidates for adjuvant treatment trials.

Key Words: nomograms, prostatic neoplasms, prostatectomy, recurrence, prognosis

Abbreviations and Acronyms

BCR = biochemical recurrence
CC = Cleveland Clinic
ECE = extracapsular extension
PSA = prostate specific antigen
RP = radical prostatectomy
SVI = seminal vesicle invasion

Submitted for publication June 23, 2008.

Study received approval from local institutional review boards.

* Correspondence: Department of Urology, Institut Paoli-Calmettes, 232 Boulevard Ste. Marguerite, PO Box 156, 13273 Marseille, France (telephone: +33-491223532; FAX: +33-491223613; e-mail: walzj@marseille.fnclcc.fr).

† Supported by the Grant of the Vereinigung Norddeutscher Urologen.

‡ Supported by the University of Montreal Heath Center Urology Associates, Fonds de la Recherche en Santé du Québec, the University of Montreal Department of Surgery and the University of Montreal Health Center (CHUM) Foundation.

Approximately 25% of all patients undergoing radical prostatectomy for localized prostate cancer will experience BCR during followup.[1,2] Two-thirds of BCR is early during the first 2 years after RP.[3] An early recurrence after RP usually implies a biologically more aggressive prostate cancer and poor prognosis. This might be related to the presence of occult metastatic disease or locally advanced disease.[3–5] Pound et al demonstrated

0022-5347/09/1812-0601/0
THE JOURNAL OF UROLOGY®
Copyright © 2009 by American Urological Association
Vol. 181, 601-608, February 2009
Printed in U.S.A.
DOI:10.1016/j.juro.2008.10.033

that patients with BCR during the first 2 years after RP have a 20% higher rate of metastatic progression at 5 years compared to those with more delayed BCR.[5] Freedland et al demonstrated that time to recurrence also represents an important predictor of prostate cancer specific mortality, where recurrence within 3 years after RP increased the risk of cause specific mortality by a factor of 3.5.[4,6] These data represent examples of the adverse prognostic characteristics associated with early recurrence and imply that particularly aggressive therapy might be necessary in these patients.[5,7–10] To date to our knowledge there is no tool available that is capable of prospectively assigning the risk of early recurrence to an individual patient. This may render the delivery of adjuvant therapy difficult. Currently available tools only predict the cumulative probability of disease relapse within 5 or 10 years.[11–14] To address this issue we developed a nomogram predicting the probability of early recurrence defined as BCR within 2 years after RP and externally validated this tool in an independent data set.

MATERIALS AND METHODS

Patient Population

Between 1992 and 2005, 3,310 patients underwent open retropubic RP for prostate cancer without neoadjuvant hormonal therapy in Hamburg, Germany. Due to missing values for predictor variables 399 patients were excluded from analysis. This left complete records for 2,911 patients who represented the development cohort. A second cohort of 2,875 patients treated with open retropubic RP at the Cleveland Clinic between 1987 and 2005 was used for independent validation. Standard lymphadenectomy was performed according to the institution policy. In the development cohort 40.9% (1,191) and in the validation cohort 49.3% (1,417) did not undergo lymphadenectomy. At both centers clinical stage was assigned by the attending urologist according to the 2002 TNM system. Pretreatment PSA was measured before digital rectal examination or prostate ultrasound. In the Hamburg cohort pretreatment and followup PSA was mainly determined by the ultrasensitive monoclonal Immulite® DPC immunoassay (1995 to 2000) and by the Abbott AxSYM® PSA assay (2000 to present). In the Cleveland cohort the Hybritech PSA assay was used principally for both evaluations. Biopsy and pathological grading were performed by dedicated genitourinary pathologists according to the Gleason system. Pathological stage was defined according to the Partin criteria, namely organ confined, ECE, SVI and lymph node invasion.[15] A positive surgical margin was defined as cancer cells in contact with the inked surface of the specimen. Depending on institutional policy followup consisted of quarterly to biannual visits during the first year, biannual visits from years 2 to 5 and annual visits thereafter. In the Hamburg cohort BCR was defined as a postoperative PSA of 0.1 ng/ml and increasing vs 0.2 ng/ml and increasing in the CC cohort. None of the patients in these cohorts received adjuvant treatment after initial RP until relapse. The study was performed after approval by local institutional review boards.

Statistical Analyses

The Hamburg cohort was used for model development. Estimates of the probability of remaining free of BCR were calculated using the Kaplan-Meier method. Univariable and multivariable Cox proportional hazards regression models were used to identify significant predictors of BCR. Predictors consisted of age, PSA, pathological Gleason sum, ECE, SVI, surgical margin status and lymph node invasion. Pathological Gleason sum was categorized into Gleason 6 or less, 7 and 8 or greater. Age was excluded from multivariable analyses due to its lack of statistical significance in the univariable models. A nomogram predicting BCR-free survival specifically within 2 years after RP was based on the multivariable model. For the validation of the model discrimination and calibration were assessed in the CC data set. The c-index was used to assess discrimination and was expressed as a value between 0.5 and 1.0, where 1.0 indicates perfect predictions and 0.5 is equivalent to a toss of a coin. To generate the c-index the nomogram predicted probability of BCR-free survival was compared with the actual outcome of patients in the external validation cohort. The relationship between the nomogram predicted probability and the observed fraction of BCR-free survival at 2 years was graphically depicted in the calibration plot.

Finally, we tested various nomogram probability cutoffs to assess its ability to identify patients with or without early BCR. Patients in the external validation cohort who were free of BCR but had a followup shorter than 2 years (813) were excluded from this part of the analysis, resulting in a subcohort of 2,062, of which 257 (12.5%) were recorded as having BCR within the first 2 years. These cutoffs were then compared to predictions based on pathological disease stage at RP as those characteristics are currently the standard indicator of the need for adjuvant therapy after RP.[7,8,16] All statistical tests were performed using S-PLUS® Professional, version 1. All tests were 2-sided with a significance level set at 0.05.

RESULTS

The patient characteristics of the 2 cohorts are shown in table 1. In the development cohort complete 2-year followup was available for 1,528 (52.5%) patients. Within 2 years 381 (13.1%) patients had BCR, which represented 63.7% of all BCR in this cohort (598). Of the latter patients 75 (12.5%) had BCR diagnosed at 3 months after RP. Actuarial BCR-free survival at 2 years was 83.6% (95% CI 82.1 to 85.2). In the CC validation cohort complete 2-year followup was available for 1,806 (62.8%) patients. Within 2 years BCR developed in 257 (8.9%) patients, which represented 52.2% of all BCR in this cohort (494). Of these patients 82 (16.6%) had BCR diagnosed at 3 months after RP. Actuarial BCR-free survival at 2 years was 89.6% (95% CI 90.8 to 88.4).

Download English Version:

https://daneshyari.com/en/article/3871340

Download Persian Version:

https://daneshyari.com/article/3871340

Daneshyari.com