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DEVELOPMENT AND VALIDATION OF A NOMOGRAM PREDICTING THE OUTCOME OF PROSTATE BIOPSY BASED ON PATIENT AGE, DIGITAL RECTAL EXAMINATION AND SERUM PROSTATE SPECIFIC ANTIGEN

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Abstract

Purpose—We developed and validated a nomogram which predicts presence of prostate cancer (PCa) on needle biopsy.

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Materials and Methods—We used 3 cohorts of men who were evaluated with sextant biopsy of the prostate and whose presenting prostate specific antigen (PSA) was not greater than 50 ng/ml. Data from 4,193 men from Montreal, Canada were used to develop a nomogram based on age, digital rectal examination (DRE) and serum PSA. External validation was performed on 1,762 men from Hamburg, Germany. Data from these men were subsequently used to develop a second nomogram in which percent free PSA (%fPSA) was added as a predictor. External validation was performed using 514 men from Montreal. Both nomograms were based on multivariate logistic regression models. Predictive accuracy was evaluated with areas under the receiver operating characteristic curve and graphically with loess smoothing plots.

Results—PCa was detected in 1,477 (35.2%) men from Montreal, 739 (41.9%) men from Hamburg and 189 (36.8%) men from Montreal. In all models all predictors were significant at 0.05. Using age, DRE and PSA external validation AUC was 0.69. Using age, DRE, PSA and %fPSA external validation AUC was 0.77.

Conclusions—A nomogram based on age, DRE, PSA and %fPSA can highly accurately predict the outcome of prostate biopsy in men at risk for PCa.

Keywords

prostatic neoplasms; biopsy; nomograms; validation studies

Prostate cancer (PCa) is a significant cause of morbidity and mortality. In the United States PCa is the most common cancer and the second most common cause of cancer-related death. In 2003 an estimated 220,900 new cases and 28,900 deaths from PCa were recorded. Similar data have been reported in Europe and Canada. Increasing PCa awareness motivates patients to seek the most objective information regarding the probability of PCa diagnosis. After an abnormal screening test many men face the prospect of prostate biopsy and wish to know the odds of harboring PCa. Similarly physicians may wish to estimate the probability of positive biopsy when biopsy is recommended. Despite being accustomed to the notion of increased risk of PCa, referring physicians may have difficulty in estimating the risk for individual patients. While several risk factors for prostate cancer have been identified, their combined, multivariate and most bias-free contribution may be difficult to quantify. Nomograms have been introduced to circumvent this difficulty.¹⁻¹² Nomograms quantify the combined contribution of several risk factors and provide a predicted probability of the event of interest. Their prediction applies to an individual instead of situating this individual within a risk group.^{1-3, 13}

Several authors explored the application of predictive models for estimation of risk of PCa on needle biopsy.^{1-3, 13} Eastham et al have shown that in men with abnormal digital rectal examination (DRE) and serum prostate specific antigen (PSA) less than 4.0 ng/ml, a nomogram has a predictive accuracy of 75%.¹³ We decided to complement this and other contributions by developing a nomogram which also applies to men with suspicious DRE findings and may be used across all PSA values. Moreover we tested whether the addition of percent free PSA (%fPSA) would enhance nomogram predictive accuracy.

MATERIALS AND METHODS

Patient population

Three patient cohorts were used for development and validation. Within these cohorts most men were referred for a prostatic evaluation because of suspicious DRE, and/or abnormal PSA or free PSA. The first cohort consisted of 4,193 men evaluated with sextant needle biopsy in Montreal, Canada between February 1990 and March 1998. Serum PSA was measured in all subjects before DRE and transrectal ultrasound (TRUS) guided biopsy. DRE findings were

classified as normal or suspicious for cancer. Systematic sextant biopsies were performed as described elsewhere.^{14,15}

The second cohort consisted of 514 patients from Montreal, Canada. All men were evaluated between January 1998 and October 1999 using the same criteria as the first cohort. Percent free PSA was added to their assessment.¹⁵

The third cohort consisted of 1,762 men assessed with ultrasound guided sextant biopsy of the prostate between January 1992 and March 2000 at the University Hospital Hamburg-Eppendorf, Germany. Serum PSA and free PSA (fPSA) levels were measured in all subjects before DRE and TRUS. DRE findings were classified as normal or suspicious for cancer. Systematic biopsies were performed using the same template as for the 2 other cohorts.^{14,15} In all 3 cohorts no patient had a total PSA before biopsy greater than 50 ng/ml since that cutoff is considered 98.5% accurate in predicting the presence of PCa on needle biopsy.¹⁶

The Montreal cohort of 4,193 men was used to develop a nomogram predicting the probability of PCa on needle biopsy using age, DRE and PSA. The Hamburg cohort of 1,762 men was used for validation of this nomogram. The Hamburg cohort was subsequently used to develop a nomogram predicting the probability of PCa on needle biopsy using age, DRE, PSA and fPSA. Finally this nomogram was validated on the Montreal cohort of 522 men.

Statistical analyses

Statistical tests were performed using SPSS® version 10 and S-PLUS® Professional version 1. Two-sided tests with significance at 0.05 were used. For each nomogram the association between predictors and PCa on needle biopsy was tested in multivariate logistic regression models. Predictive accuracy of the nomograms was quantified with the area under the receiver operating characteristic curve (AUC). The extent of overestimation or underestimation of the observed PCa biopsy rate was explored graphically with a nonparametric, local regression smoothing technique.

RESULTS

Patient characteristics according to cohorts of origin are shown in table 1. Table 2 shows the multivariate logistic regression models of age, DRE, PSA and %fPSA. All variables were statistically significant predictors of PCa on needle biopsy (all p [H11021]0.05). Figure 1 shows the nomograms and table 3 shows predictive accuracy. The nomogram based on age, DRE, PSA and fPSA showed noticeably better external validity (0.77, 95% CI 0.72-0.81) than the nomogram using age, DRE and PSA (0.69, 95% CI 0.68 - 0.72).

Loess plots of performance characteristics are shown in figure 2 and demonstrate that both nomograms show departures from ideal predictions. For example the age, DRE and PSA nomogram demonstrated an area of overestimation of the actual probability for predicted values between 30% and 50%. The nomogram, which also incorporates %fPSA, demonstrated an area of overestimation for predicted probabilities of 20% to 40% and 85% to 100%.

DISCUSSION

In this study we developed and validated 2 nomograms predicting the probability of PCa on needle biopsy in men referred for prostate biopsy. Using age, DRE and PSA the prediction AUC is 69%. Adding a more specific PSA variant such as %fPSA enhances the AUC to 77%. Therefore, in 100 sets of randomly paired patients in which 1 has PCa on needle biopsy and the other does not, the nomograms would correctly predict who has PCa in 69% and 77%.

As shown in table 4 these results compare extremely favorably with previously reported regression based nomograms for patients with localized PCa.¹⁻¹³ This favorable comparison relates to the nature of the predictor variables used in the current nomograms, namely age, DRE, PSA and fPSA. These predictors are less informative and less reliable than biopsy Gleason grade, or pathological grade and stage variables. Despite this limitation our %fPSA based nomogram predicted more accurately than nomograms which address biochemical recurrence after brachytherapy or external beam radiotherapy,^{6,7} and nearly equaled the accuracy of the preoperative biochemical recurrence nomogram.^{4,5} These observations suggest that the outcome of prostate needle biopsy is at least as predictable as PCa biochemical recurrence after definitive therapy.⁴⁻¹² More-over the predictive accuracy of needle biopsy nomograms is generalizable as demonstrated by our external validation results. These remained virtually unchanged relative to development samples at 69% vs original 70% for the age, DRE and PSA based nomogram, and 77% vs original 78% for the age, DRE, PSA and %fPSA based nomogram. These external validity estimates demonstrated less pronounced differences between development and external validation samples than were observed for the preoperative and postoperative nomograms of PCa bio-chemical recurrence.^{4,8,10,11} Preoperative PSA recurrence accuracy estimates ranged from 0.67 to 0.83 vs the original AUC of 0.79, and postoperative accuracy ranged from 0.77 to 0.82 vs the original AUC of 0.89.

Our results complement several important contributions.^{1-3,13,17,18} Carlson¹⁷ and Potter¹⁸ et al published algorithms combining different clinical variables to predict the presence of PCa on needle biopsy. Carlson et al presented sensitivity and specificity values for a subcohort of patients. However, they failed to show AUC based predictive accuracy estimates.¹⁷ Lack of predictive accuracy testing represents an important limitation of this contribution and precludes the safe implementation of this model under novel testing conditions. Sensitivity and specificity values provided by the authors depend on disease prevalence and are difficult to compare between populations in which prevalence may differ. This notion is particularly important in PCa early detection, where PCa risk may differ sharply between a referred population such as ours vs men from the general population. Use of AUC derived estimates of predictive accuracy by-passes the limitations of sensitivity and specificity since predictive accuracy does not differ across populations.

Eastham et al have shown that the combination of age, race and PSA yields an AUC of 75% in prediction of PCa on needle biopsy.¹³ Despite good accuracy the Eastham et al nomogram suffers from limited generalizability. It was tested and validated in men with suspicious DRE findings and serum PSA less than 4.0 ng/ml. Therefore, the nomogram cannot be applied to men with unremarkable DRE findings and does not apply to PSA greater than 4.0 ng/ml. Recently Garzotto et al developed a nomogram predicting PCa on needle biopsy using routinely available clinical and TRUS variables which yielded a predictive accuracy of 73%.¹ Despite adequate predictive accuracy this model has 2 important limitations. Use of ultrasound based input is highly impractical since men who undergo transrectal ultrasound are also likely to undergo ultrasound guided needle biopsy. Moreover the predictions of this nomogram are only applicable after TRUS since TRUS variables are necessary for risk estimation. Therefore, predictions based on input that does not require ultrasound findings are more practical and may be interpreted before planned ultrasound guided biopsy. Moreover despite the added input from TRUS, this nomogram demonstrated minimal increase in predictive accuracy relative to our nomogram which relies on age, DRE and PSA (73% vs 69%), and was apparently inferior to our %fPSA based nomogram (73% vs 77%).

Lack of graphic exploration of the performance characteristics of these nomograms represents another limitation.^{1,2} The importance of performance characteristics testing is emphasized by our data. These demonstrated apparently acceptable predictive accuracy of the age, DRE and PSA based nomogram at 69%. Exploration of the performance characteristics shows that for

predicted values from 0% to 30% the nomogram underestimates the observed rate of PCa, for values from 30% to 50% the nomogram overestimates and for values from 70% to 100% the model underestimates again (fig. 1). Therefore, unless predictive accuracy is close to 100% it is imperative to know for which values a predictive tool may provide a falsely low or a falsely high prediction.

Djavan et al used artificial neural networks (NN) to develop a predictive model which among other variables relies on TRUS data.² The need for TRUS input limits the applicability of this tool in a fashion similar to that of Garzotto et al.¹ Moreover the nature of NN limits their practical applicability. These models are not amenable to a paper based, portable and clinically applicable format. NN require computer support since complex calculations are necessary. Therefore, they cannot be distributed to a wide array of clinical users in a format similar to PCa nomograms.^{4,10} Additionally NN based predictions may be artificially high due to potential data over fit. Finally the performance characteristics of NN cannot be assessed. Therefore, it cannot be known whether NN under estimate or over estimate the observed outcome for specific prediction ranges.

Regression based nomograms such as ours may be superior to mental predictions. Clinicians rely on personal knowledge and previous experience with similar cases to estimate the outcome of interest. These factors may contribute to highly subjective input and may result in important interobserver and intraobserver variability. Moreover when clinicians are faced with complex prediction situations, they tend to generate mental predictions that stratify risk between low and high rather than estimating an exact numeric value. This form of stratification may be conceptually less challenging than estimation of a numerical value. Nomograms may obviate that difficulty and may provide a relatively bias-free estimate of individual risk. Nomograms such as ours rely on fewer input sources than the numerous inputs processed by clinicians. Clinicians likely process numerous objective and subjective variables. The subjective inputs may be conscious while others may be subconscious. Despite fewer input variables of lesser complexity, regression based nomograms have been shown to perform equally well compared to expert physician predictions.^{19,20} Nomogram applications addressing disease models others than PCa have demonstrated better performance than expert physicians.²⁰ It is noteworthy that the participants of nomogram vs clinician comparisons in PCa consisted of highly trained urological oncologists with a particular interest in nomogram development. This may have biased clinician estimates toward higher accuracy compared with nonexperts such as general urologists or clinicians from allied, albeit nonurological, fields (medical oncologists, radiation oncologists, etc). Therefore, comparisons between nonexpert clinicians may yield results that favor nomogram based predictions.

Several limitations may apply to this study. Our data did not contain information on race and virtually all men were white. The omission of race may limit the applicability of the nomogram to nonwhite men.^{2,4} Moreover the 3 cohorts used in our study represent high risk populations. Men from Montreal and Hamburg were referred for sextant prostate biopsy and their characteristics are different from those of a screening population. Therefore, this nomogram should ideally be applied to men identified as high risk and referred for prostatic evaluation. The nomogram only applies to men who present for a first biopsy since patients undergoing repeat biopsy were not included in this analysis. Alternatively the nomogram could be applied to men in whom a referral is contemplated. Finally we wish to emphasize that prostate biopsies are limited by the extent of sampling and do not invariably reflect true disease status.

CONCLUSIONS

We have developed and validated 2 nomograms, which predict the presence of PCa on sextant needle biopsy. The nomogram based on age, DRE and PSA provides intermediate predictive

accuracy compared with existing predictive tools. Conversely the nomogram based on age, DRE, PSA and %fPSA provides high predictive accuracy which is combined with good performance characteristics. Both nomograms are based on routinely available clinical variables and do not require TRUS. Moreover the nomograms are amenable to a paper based format. Finally they can be adapted for use in the Palm OS® environment and they are currently available on the Internet (www.auq.org) free of charge.

REFERENCES

1. Garzotto M, Hudson RG, Peters L, Hsieh YC, Barrera E, Mori M, et al. Predictive modeling for the presence of prostate carcinoma using clinical, laboratory, and ultrasound parameters in patients with prostate specific antigen levels ≤ 10 ng/mL. *Cancer* 2003;98:1417. [PubMed: 14508828]
2. Djavan B, Remzi M, Zlotta A, Seitz C, Snow P, Marberger M. Novel artificial neural network for early detection of prostate cancer. *J Clin Oncol* 2002;20:921. [PubMed: 11844812]
3. Lopez-Corona E, Ohori M, Scardino PT, Reuter VE, Gonen M, Kattan MW. A nomogram for predicting a positive repeat prostate biopsy in patients with a previous negative biopsy session. *J Urol* 2003;170:1184. [PubMed: 14501721]
4. Bazinet M, Meshref AW, Trudel C, Aronson S, Peloquin F, Nachabe M, et al. Prospective evaluation of prostate specific antigen density and systematic biopsies for early detection of prostatic carcinoma. *Urology* 1994;43:44. [PubMed: 7506853]
5. D'Amico AV, Whittington R, Malkowicz SB, Fondurulia J, Chen MH, Kaplan I, et al. Pretreatment nomogram for prostate-specific antigen recurrence after radical prostatectomy or external-beam radiation therapy for clinically localized prostate cancer. *J Clin Oncol* 1999;17:168. [PubMed: 10458230]
6. Kattan MW, Zelefsky MJ, Kupelian PA, Scardino PT, Fuks Z, Leibel SA. Pretreatment nomogram for predicting the outcome of three-dimensional conformal radiotherapy in prostate cancer. *J Clin Oncol* 2000;18:3352. [PubMed: 11013275]
7. Kattan MW, Potters L, Blasko JC, Beyer DC, Fearn P, Cavanagh W, et al. Pretreatment nomogram for predicting freedom from recurrence after permanent prostate brachytherapy in prostate cancer. *Urology* 2001;58:393. [PubMed: 11549487]
8. Graefen M, Karakiewicz PI, Cagiannos I, Hammerer PG, Haese A, Palisaar J, et al. A validation of two preoperative nomograms predicting recurrence following radical prostatectomy in a cohort of European men. *Urol Oncol* 2002;7:141. [PubMed: 12474529]
9. Graefen M, Karakiewicz PI, Cagiannos I, Quinn DI, Henshall SM, Grygiel JJ, et al. International validation of a preoperative nomogram for prostate cancer recurrence after radical prostatectomy. *J Clin Oncol* 2002;20:3206. [PubMed: 12149292]
10. Kattan MW, Wheeler TM, Scardino PT. Postoperative nomogram for disease recurrence after radical prostatectomy for prostate cancer. *J Clin Oncol* 1999;17:1499. [PubMed: 10334537]
11. Graefen M, Karakiewicz PI, Cagiannos I, Klein E, Kupelian PA, Quinn DI, et al. Validation study of the accuracy of a postoperative nomogram for recurrence after radical prostatectomy for localized prostate cancer. *J Clin Oncol* 2002;20:951. [PubMed: 11844816]
12. Graefen M, Ohori M, Karakiewicz PI, Cagiannos I, Hammerer PG, Haese A, et al. Assessment of the enhancement in predictive accuracy provided by systematic biopsy in predicting outcome for clinically localized prostate cancer. *J Urol* 2004;171:200. [PubMed: 14665876]
13. Eastham JA, May R, Robertson JL, Sartor O, Kattan MW. Development of a nomogram that predicts the probability of a positive prostate biopsy in men with an abnormal digital rectal examination and a prostate-specific antigen between 0 and 4 ng/mL. *Urology* 1999;54:709. [PubMed: 10510933]
14. Tanguay S, Begin LR, Elhilali H, Behlouli H, Karakiewicz PI, Aprikian AG. Comparative evaluation of total PSA, free/total PSA, and complexed PSA in prostate cancer detection. *Urology* 2002;59:261. [PubMed: 11834399]
15. Kattan MW, Eastham JA, Stapleton AM, Wheeler TM, Scardino PT. A preoperative nomogram for disease recurrence following radical prostatectomy for prostate cancer. *J Natl CancerInst* 1998;90:766.

16. Gerstenbluth RE, Seftel AD, Hampel N, Oefelein MG, Resnick MI. The accuracy of the increased prostate specific antigen level (greater than or equal to 20 ng./ml.) in predicting prostate cancer: is biopsy always required? *J Urol* 2002;168::1990. [PubMed: 12394692]
17. Carlson GD, Calvanese CB, Partin AW. An algorithm combining age, total prostate-specific antigen (PSA), and percent free PSA to predict prostate cancer: results on 4298 cases. *Urology* 1998;52::455. [PubMed: 9730460]
18. Potter SR, Horniger W, Tinzi M, Bartsh G, Partin AW. Age, prostate specific antigen, and digital rectal examination as determinants of the probability of having prostate cancer. *Urology* 2001;57::1100. [PubMed: 11377318]
19. Graefen M, Augustin H, Palisaar J, Haese A, Michl U, Noldus J, et al. Who predicts better: a clinician or a nomogram? *J Urol*, suppl 2003;169::293.abstract 1140
20. Ross PL, Gerigk C, Gonen M, Yossepowitch O, Cagiannos I, Sogani PC, et al. Comparisons of nomograms and urologists' predictions in prostate cancer. *Semin Urol Oncol* 2002;20::82. [PubMed: 12012293]

FIG. 1.

Nomograms predicting probability of PCa on needle biopsy using age, DRE, serum PSA and %fPSA. DRE 0, benign. DRE 1, suspicious for PCa. perc.fPSA, %fPSA. P[PCa on needle biopsy], probability of prostate cancer on needle biopsy.

FIG. 2.

Local regression nonparametric smoothing plots which show performance of nomograms relative to observed rates of PCa diagnosis on needle biopsy. X-axes represent nomogram predicted probability of PCa on needle biopsy. Y-axes represent observed rate of PCa diagnosis with sextant prostate biopsy. Within each panel perfect prediction would correspond to slope of 1 (diagonal 45-degree broken line). Solid line indicates observed (apparent) nomogram performance.

TABLE 1

Baseline clinical characteristics of patients who underwent systematic sextant biopsy

	Montreal Cohort	Hamburg Cohort	Montreal Cohort
No. pts	4,193	1,762	514
Age:			
Mean	64.2	64.8	63.2
Median	65.0	64.0	63.0
Range	34-85	17-88	45-83
PSA:			
Mean	9.8	8.9	8.1
Median	7.9	7.1	6.4
Range	0-50	0-50	0-50
%fPSA:			
Mean	—	0.17	0.19
Median	—	0.15	0.18
Range	—	0.01-0.91	0-0.83
No. suspicious DRE (%)	1,561 (37.2)	294 (16.7)	156 (30.4)
No. prostate Ca on needle biopsy (%)	1,477 (35.2)	739 (41.9)	189 (36.8)

TABLE 2

Multivariate logistic regression models

	Regression Coefficient	p Value
Nomogram 1:		
Age	0.02071	<0.001
Suspicious DRE	1.24486	<0.001
PSA (ng/ml)	0.05563	<0.001
Intercept	-3.01038	<0.001
Nomogram 2:		
Age	0.02436	0.001
Suspicious DRE	1.82162	<0.001
PSA (ng/ml)	0.02858	<0.001
%fPSA	-8.68001	<0.001
Intercept	-1.01469	0.03

For nomogram 1 the regression coefficients reflect the association between predictors and prostate cancer on needle biopsy in 4,193 men from Montreal.

For nomogram 2 the regression reflects the association between predictors and prostate cancer on needle biopsy in 1,762 men from Hamburg.

TABLE 3
Accuracy of nomograms predicting presence of PCa on needle biopsy

	AUC	95% CI
Nomogram 1—age, PSA + DRE:		
Montreal development cohort	0.70	0.68-0.72
Hamburg external validation cohort	0.69	0.68-0.72
Nomogram 2—age, PSA, DRE + %fPSA:		
Hamburg development cohort	0.78	0.75-0.80
Montreal external validation cohort	0.77	0.72-0.81

Accuracy was quantified with AUC and is accompanied by its 95% confidence interval (CI).

TABLE 4

Predictive accuracy of various PCa nomograms

References		AUC
<i>Prediction of PCa on needle biopsy</i>		
Eastham et al ¹³	Age, race, DRE, PSA (0-4 ng/ml)	0.75
Garzotto et al ¹	Age, race, family history, referral indications, prior vasectomy, DRE, PSA (10 ng/ml or less), TRUS findings	0.73
Djavan et al ²	PSA, %fPSA, TRUS findings	0.88-0.91
Lopez-Corona et al ³	Age, family history, PSA, PSA slope, DRE, mos from initial biopsy, cumulative No. previous neg cores, history of high grade prostatic intraepithelial neoplasia or atypical small acinar proliferation	0.70
Present study	Age, PSA, DRE	0.69
	Age, PSA, %fPSA, DRE	0.77
<i>Pretreatment predictors of biochemical recurrence</i>		
Kattan et al ¹⁵	PSA, stage, biopsy Gleason sum	0.79
D'Amico et al ⁵	PSA, stage, biopsy Gleason sum	—
Kattan et al ⁶	PSA, stage, biopsy Gleason sum, neoadjuvant androgen therapy, radiation dose	0.76
Kattan et al ⁷	PSA, stage, biopsy Gleason, external beam radiation	0.61-0.64
Graefen et al ⁸	External validation of Kattan et al nomogram ¹⁵	0.83
Graefen et al ⁸	External validation of D'Amico et al nomogram ³	0.80
Graefen et al ⁹	External validation of Kattan nomogram	0.67-0.83
<i>Posttreatment predictors of biochemical recurrence</i>		
Kattan et al ¹⁰	PSA, biopsy Gleason, surgical margins, extracapsular extension, seminal vesicle invasion, lymph node invasion	0.89
Graefen et al ¹¹	External validation of Kattan et al nomogram ¹⁰	0.77-0.82
Graefen et al ¹²	PSA, stage, biopsy Gleason, biopsy information	0.79-0.81