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# A New Nomogram to Predict Pathologic Outcome Following Radical Prostatectomy

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**ABSTRACT**

*Objective:* To develop a preoperative nomogram to predict pathologic outcome in patients submitted to radical prostatectomy for clinical localized prostate cancer.
*Materials and Methods:* Nine hundred and sixty patients with clinical stage T1 and T2 prostate cancer were evaluated following radical prostatectomy, and 898 were included in the study. Following a multivariate analysis, nomograms were developed incorporating serum PSA, biopsy Gleason score, and percentage of positive biopsy cores in order to predict the risks of extraprostatic tumor extension, and seminal vesicle involvement.
*Results:* In univariate analysis there was a significant association between percentage of positive biopsy cores ($p < 0.001$), serum PSA ($p = 0.001$) and biopsy Gleason score ($p < 0.001$) with extraprostatic tumor extension. A similar pathologic outcome was seen among tumors with Gleason score 7, and Gleason score 8 to 10. In multivariate analysis, the 3 preoperative variables showed independent significance to predict tumor extension. This allowed the development of nomogram-1 (using Gleason scores in 3 categories - 2 to 6, 7 and 8 to 10) and nomogram-2 (using Gleason scores in 2 categories - 2 to 6 and 7 to 10) to predict disease extension based on these 3 parameters. In the validation analysis, 87% and 91.1% of the time the nomograms-1 and 2, correctly predicted the probability of a pathological stage to within 10% respectively.
*Conclusion:* Incorporating percent of positive biopsy cores to a nomogram that includes preoperative serum PSA and biopsy Gleason score, can accurately predict the presence of extraprostatic disease extension in patients with clinical localized prostate cancer.

***Key words**: prostatic neoplasms; neoplasm staging; nomograms; prostate-specific antigen; needle biopsy*
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## INTRODUCTION

Gleason grade from biopsy, along with serum PSA and tumor extent at digital rectal examination, are the current most common parameters used to predict the risk of organ confined disease and choose a definitive treatment in patients with prostate cancer (1).

However, some studies show that clinical stage as defined at digital rectal examination is neither the ideal method to choose a definitive therapy (2) nor to predict biochemical outcome after treatment (3-6). The percentage of patients staged as T1c increased from less than 1% in the eighties to 60% in the nineties. Furthermore, a study of more than 1000 patients that underwent radical retropubic

prostatectomy did not find statistical difference in disease recurrence rates among patients staged as T2a, T2b or T2c at digital rectal examination after a 10 years follow up period (7).

New variables to predict the probabilities of organ confined disease and disease recurrence after treatment have been widely studied (8-10), and the percentage of positive biopsy cores (PPBC) for cancer has emerged as an independent prognostic factor (11-13). Probably, the reason for this importance is based on its straight relation with tumor volume in radical prostatectomy specimens (14).

As discussed above, several individual parameters have the power to preoperatively predict the risk of the actual pathologic stage and biochemical outcome after treatment. For this reason, many authors have analyzed the use of pre- and postoperative nomograms in order to find patients in which a high risk of extra-prostatic disease (15) or high rates of disease progression are expected (16,17).

The first nomogram developed by Partin et al. (18), to predict the risks of nomogram confined disease and involvement of seminal vesicles and iliac lymph nodes in patients that underwent radical retropubic prostatectomy, included the biopsy Gleason score, clinical stage and serum PSA levels.

Considering that the percent positive biopsy cores represent an important prognostic factor (19), clinical stage as defined at digital rectal examination is not as relevant as it was thought before (4) and some studies incorporated the PPBC into models of prognostic value (8), in the present study we analyzed the predictive power of a new nomogram including the preoperative serum PSA and the biopsy Gleason score along with the PPBC.

## MATERIALS AND METHODS

Between September 1988 and December 2002, 960 patients with clinically localized prostate cancer who underwent radical retropubic prostatectomy were retrospectively studied. All the patients underwent clinical and pathological staging according to the TNM staging system (20).

From the 960 patients, only those men with complete information regarding the total number of biopsy cores, number of fragments with cancer, biopsy Gleason score, serum PSA levels and pathologic analysis of the surgical specimen were studied. Fifty-four patients that received neoadjuvant androgen deprivation therapy or were diagnosed through transurethral resection or transvesical prostatectomy were excluded. A total of 898 remained in study. Table-1 shows the patients characteristics.

The same surgeon (MS) performed all the surgical procedures according to the Walsh technique (21), modified by Srougi (22). The same pathologist (KRL) analyzed all the surgical specimens, including the prostate gland, seminal vesicles and obturatory lymph.

### Macroscopic Analysis

The specimens of radical prostatectomy were fixed in buffered formalin 10% for a period of 6h. After weighting and measuring the gland, thin transversal sections were performed in the surgical margins related to the bladder neck and the prostate apex. The seminal vesicles were sectioned in the base and longitudinal sections were submitted to histological examination. The entire gland was included for study after having their margins painted with India ink. The right and left lobes were separated, with sequential transversal sections being performed every 3 mm, designed from the proximal region towards the distal one. Between 10 and 12 sections from each lobe were included for histological study. The lymph nodes from the fat related to the resection of the iliac chain were dissected and sections representative of each nodular structure were included for study.

### Microscopic Analysis

The specimens underwent the usual processing with inclusion in paraffin. Sections of 4 to 6 mm were stained by hematoxylin-eosin. The analyzed parameters were:

Histological pattern and Gleason score - The Gleason histological grade was used for evaluating the histological differentiation, considering only the acinar pattern (23).

***Table 1*** *– Demographic and clinical features of the 898 patients.*

| | |
|---|---|
| **N Patients** | 898 |
| **Age** (years) | |
| Mean ± SD | 62.9 ± 7.4 |
| Median | 63.5 |
| Minimum – maximum | 40 - 83 |
| **PSA** (ng/mL) | |
| Mean ± SD | 10.1 ± 7.3 |
| Median | 8.0 |
| Minimum – Maximum | 0.3 - 63.5 |
| 0 to 4.0 | 84 (9.4%) |
| 4.1 to 10.0 | 512 (57.0%) |
| 10.1 to 20.0 | 236 (26.3%) |
| > 20.0 | 66 (7.3%) |
| **Gleason** | |
| 2 to 6 | 653 (72.7%) |
| 7 | 165 (18.4%) |
| 8 to 10 | 80 (8.9%) |
| **Clinical Stage** | |
| T1c | 432 (48.1%) |
| T2 | 459 (51.1%) |
| T3a | 7 (0.8%) |
| **Pathologic Stage** | |
| T2 | 599 (66.7%) |
| T3 | 296 (33.0%) |
| T4 | 3 (0.3%) |
| **Total Number of Cores** | |
| Mean ± SD | 8.1 ± 3.3 |
| Median | 7.0 |
| Minimum – maximum | 2.0 - 22.0 |
| **Number of Positive Cores** | |
| Mean ± SD | 3.2 ± 2.1 |
| Median | 3.0 |
| Minimum – maximum | 1.0 - 20.0 |
| **Percent Positive Biopsy Cores** | |
| Mean ± SD | 41.2% ± 24.1% |
| Median | 33.3% |
| Minimum – maximum | 5.0% - 100.0% |
| 0 to 25.0% | 290 (32.3%) |
| 25.1 to 50.0% | 392 (43.7%) |
| 50.1 to 75.0% | 134 (14.9%) |
| 75.1 to 100.0% | 82 (9.1%) |

Surgical margins - Positive margin was defined if carcinoma was within the bladder neck or distal urethral shave tissues, or if India ink was identified on tumor cells at a peripheral margin.

Extra-prostatic involvement - The invasion of adipose tissue and the periprostatic neurovascular plexus was considered as involvement of extra-prostatic tissue and, therefore, non organ-confined disease.

Seminal vesicle involvement - The involvement of seminal vesicle parenchyma and not only the adventitial tissue was considered seminal vesicle involvement.

Lymph node metastasis - The obturatory lymph nodes involved with cancer were designated as metastatic lymph nodes, and no difference regarding micro or macro-metastasis was considered.

To final analysis, the TNM 2002 (20) staging system was used.

The finding of an organ-confined disease was compared to the PPBC, serum PSA levels and Gleason score through a logistic regression model.

A multinomial logistic regression analysis (24) with 3 answers was performed: organ-confined disease, extraprostatic extension and seminal vesicle involvement. The predictive variables were the serum PSA levels, divided in categories of 0 to 4 ng/mL; 4.1 to 10.0 ng/mL; 10.1 to 20 ng/mL and greater than 20 ng/mL, the biopsy Gleason score, divided in categories of 2 to 6; 7 and 8 to 10, and then analyzed in groups of 2 to 6 and 7 to 10, and the PPBC, divided in categories of 0 to 25%; 25.1 to 50%; 50.1 to 75%; 75.1 to 100%. PPBC was defined using the formula, number of positive cores / total biopsy cores X 100.

Considering the association of the 3 parameters with disease extension on univariate and multivariate analysis, nomograms were developed based on the probabilities predicted by the adjusted model. A 95% confidence interval for the final model was obtained by repeating the analysis on 1000 bootstrap samples from the original cohort (25). The percentage of the bootstrap observed probabilities that were within 10% of the nomogram value was shown. Sensitivity, specificity, positive predictive value and negative predictive value were also determined. A significance level of 5% was adopted, and therefore, statistical significance was set as a $p \leq 0.05$. Statistical analysis was performed in the R for Windows software.

## RESULTS

Table-2 shows that number of cores retrieved from biopsy and patient age was not related to the pathologic findings of the surgical specimen. Conversely, the PPBC, biopsy Gleason score and initial PSA levels showed relation with disease extension. According to multivariate analysis, these three studied variables were independent prognostic factors for predicting prostate cancer extension (Table-2).

Table-3 shows a nomogram-1 that allows prediction of organ-confined disease according to preoperative PSA levels, biopsy Gleason score and PPBC. However, nomogram-1 also shows that if we keep unchanged the PSA and PPBC values, the confidence intervals of patients with Gleason score 7 are the same of those with Gleason score 8 to 10 regarding the finding of organ-confined disease. This fact led us to develop a nomogram-2 (Table-4), using Gleason categories of 2 to 6 and 7 to 10, without losing predictive power and making it more practical for clinical use.

A validation analysis compared the predicted probabilities from the nomogram-1 with the observed probabilities from additional 1000 bootstrap samples

***Table 2 –*** *Univariate and multivariate analysis for predicting organ-confined disease.*

| | **Univariate Analysis** | | |
|---|---|---|---|
| | **OR** | **95% CI** | **p Value** |
| **N. of cores** | 0.99 | [0.95 - 1.03] | 0.669 |
| **Age (years)** | 1.02 | [0.99 - 1.04] | 0.091 |
| **Serum PSA** | | | 0.011 |
| 4.1-10 versus 0-4.0 | 1.67 | [0.96 - 2.90] | 0.071 |
| 10.1-20 versus 0-4.0 | 2.39 | [1.33 - 4.27] | 0.003 |
| > 20.0 versus 0-4.0 | 2.38 | [1.16 - 4.89] | 0.018 |
| **Gleason** | | | < 0.001 |
| 7 / 2-6 | 3.19 | [2.25 - 4.54] | < 0.001 |
| 8-10 / 2-6 | 3.01 | [1.88 - 4.83] | < 0.001 |
| **Percentage of positive cores** | | | < 0.001 |
| 25.1-50.0 versus 0-25.0 | 1.48 | [1.05 - 2.08] | 0.025 |
| 50.1-75 versus 0-25.0 | 2.02 | [1.30 - 3.13] | 0.002 |
| 75.1-100 versus 0-25.0 | 3.94 | [2.36 - 6.58] | < 0.001 |
| | **Multivariate Analysis** | | |
| | **OR** | **95% CI** | **p Value** |
| **PSA** | | | 0.057 |
| 4.0-10 versus 0-4.0 | 1.58 | [0.89 - 2.80] | 0.120 |
| 10.0-20 versus 0-4.0 | 2.17 | [1.18 - 3.97] | 0.012 |
| > 20.0 versus 0-4.0 | 1.99 | [0.94 - 4.25] | 0.074 |
| **Gleason** | | | < 0.001 |
| 7 / 0-6 | 2.96 | [2.06 - 4.26] | < 0.001 |
| 8-10 / 2-6 | 2.86 | [1.76 - 4.64] | < 0.001 |
| **Percentage of positive cores** | | | < 0.001 |
| 25.0-50.0 versus 0-25.0 | 1.35 | [0.95 - 1.93] | 0.096 |
| 50.0-75 versus 0-25.0 | 1.58 | [0.99 - 2.50] | 0.053 |
| 75.0-100 versus 0-25.0 | 3.04 | [1.78 - 5.20] | < 0.001 |

***Table 3 – Nomogram -*** *Prediction of organ-confined disease according to preoperative PSA levels, biopsy Gleason score and percent positive biopsy cores (PPBC)**

| | Gleason Score 2 to 6 PSA (ng/mL) | | | | Gleason Score 7 PSA (ng/mL) | | | | Gleason Score 8 to 10 PSA (ng/mL) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **PPBC** | **0 to 4.0** | **4.1 to 10.0** | **10.1 to 20.0** | **> 20.0** | **0 to 4.0** | **4.1 to 10.0** | **10.1 to 20.0** | **> 20.0** | **0 to 4.0** | **4.1 to 10.0** | **10.1 to 20.0** | **> 20.0** |
| 0 to 25% | 86 (78-93) | 80 (75-85) | 75 (68-82) | 78 (65-87) | 69 (55-83) | 59 (48-69) | 51 (39-63) | 53 (35-70) | 70 (53-84) | 59 (47-71) | 52 (38-65) | x |
| 25.1 to 50% | 82 (74-90) | 75 (69-80) | 69 (61-75) | 71 (59-82) | 63 (50-77) | 51 (42-60) | 42 (31-52) | 43 (28-60) | 64 (46-79) | 52 (38-64) | 43 (30-56) | 45 (27-63) |
| 50.1 to 75% | 80 (67-90 | 72 (63-80) | 66 (55-76) | 68 (53-82) | 59 (43-76) | 47 (36-59) | 39 (27-51) | 40 (25-58) | x | 48 (33-62) | 40 (25-55) | 42 (25-61) |
| 75.1 to 100% | 72 (55-85) | 59 (46-71) | 50 (37-63) | 51 (34-67) | 46 (29-68) | 31 (21-44) | 22 (13-34) | 22 (12-37) | x | 33 (20-48) | 24 (13-38) | 24 (12-42) |

** Numbers represent percent predictive probability (95% confidence interval), X = lack of sufficient data to calculate probability.*



***Table 4 – Nomogram -*** *Prediction of organ-confined disease according to preoperative PSA levels, biopsy Gleason score and percent positive biopsy cores (PPBC)*.*

| | Gleason Score 2 to 6 PSA (ng/mL) | | | | Gleason Score 7 to 10 PSA (ng/mL) | | | |
|---|---|---|---|---|---|---|---|---|
| **PPBC** | **0 to 4.0** | **4.1 to 10.0** | **10.1 to 20.0** | **> 20.0** | **0 to 4.0** | **4.1 to 10.0** | **10.1 to 20.0** | **> 20.0** |
| 0 to 25% | 86 (78-92) | 80 (75-85) | 75 (69-82) | 78 (66-87) | 70 (57-81) | 59 (50-67) | 51 (40-62) | 54 (37-69) |
| 25.1 to 50% | 82 (75-90) | 75 (70-80) | 69 (63-76) | 71 (59-83) | 64 (51-77) | 51 (43-59) | 42 (33-52) | 44 (30-60) |
| 50.1 to 75% | 80 (68-89) | 72 (63-80) | 66 (55-75) | 68 (53-81) | 59 (43-75) | 47 (36-58) | 39 (27-51) | 41 (26-57) |
| 75.1 to 100% | 72 (57-84) | 59 (47-71) | 50 (37-62) | 51 (35-67) | 47 (29-66) | 32 (21-44) | 23 (14-33) | 23 (12-36) |

** Numbers represent percent predictive probability (95% confidence interval).*

from the study group. In the validation study, 87.0% of the time the nomograms correctly predicted the probability of a pathological stage to within 10%. The same was applied to validation of nomogram-2, which used Gleason score categories of 2 to 6 and 7 to 10. In this case, the validation study showed that in 91.1% the time the nomogram correctly predicted the probability of a pathological stage to within 10%. Tables-5 and 6 shows the sensitivity, specificity, positive predictive value, and negative predictive value achieved for various predicted probability cutoff values for organ-confined cancer when assessed in the 1000 validation bootstrap samples.

## COMMENTS

After Partin's pioneer idea of creating nomograms to predict prostate cancer extension in 1993 (18), several other models using different variables were developed to predict disease extension and/or recurrence. However, some of them are not practical for clinical use due to the complexity of its interpretation and most present a lack of significant accuracy due to the relative imprecision of the prognostic variables utilized.

Our study presents a nomogram to predict disease extension in patients with clinical localized prostate cancer on the basis of preoperative serum PSA, biopsy Gleason score and PPBC as a new parameter to be included, with more accurate results than the isolated analysis of each variable separately.

The finding of an organ-confined disease after radical retropubic prostatectomy varies from 13 to 82% of cases (18,26). In the present study, we found a 66.7% rate. This variation depends on the biopsy Gleason score, serum PSA levels and PPBC, however even with all these variables being favorable, there is still a chance of 20% of extra-prostatic extension (19).

The development of the present nomogram was not based on the clinical stage as proposed by Partin et al. (15), because we believe this variable is losing clinical significance as more than 60% of patients with prostate cancer are staged as T1c (27). This distribution differs from what was observed during the eighties, where less than 1% of cases were detected due to serum PSA level elevation (28). Furthermore, in prostate screening programs, only 10% of patients underwent transrectal needle biopsy due to abnormalities on digital rectal examination (29).

Since tumoral volume has emerged as an important prognostic factor of pathologic findings and disease recurrence, the PPBC has been used to predict pathologic (12) and biochemical outcome after treatment (19,30). This idea gained support after the demonstration of a linear relationship between PPBC and tumoral volume at radical prostatectomy specimen (31).

There is also a relation between the presence of Gleason patterns 4 or 5 on biopsy and on surgical specimens, showing that this finding at biopsy samples has prognostic value for the patient (31). In fact, 13% of the patients with biopsy Gleason score less than 7 show disease recurrence while almost 60% with a Gleason score was 7 to 10 did (32). In our series, only 48.8% of patients with a Gleason score between 8 to 10 had an organ-confined disease, while this finding occurred in 74.1% of patients with scores under 7. Thus, if we apply the nomogram in a patient with all favorable variables (PSA less than 4 ng/mL, less than 25% positive biopsy cores and Gleason score less than 7), this number reaches 86% of chances of an organ-confined disease.

When comparing patients with Gleason score 7 to patients with Gleason score 8 to 10, we noted that when keeping serum PSA values between 4 and 10 ng/mL and positive biopsy cores under 25%, the probability of finding an organ-confined disease was 60% and 61% respectively. For this reason, we decided to construct an easier nomogram considering only categories of 2 to 6 and 7 to 10. This finding demonstrates that tumors with Gleason score 7 can present a similar behavior when compared to scores 8 to 10, probably due to the fact that patients with Gleason score 7 also own different percentages of patterns 4 or even 5.

Despite all these evidences, there are still some controversies regarding cases with Gleason score 7 presenting a different behavior when compared to patients with Gleason scores 8 to 10 (33). As we know, the Gleason score 7 is composed by the

***Table 5 –*** *Predictive performance (median [95% confidence interval]) of organ-confined disease nomograms in 1000 validation bootstrap samples (nomogram-1).*

| Probability | Sensitivity, % | Specificity, % | Positive Predictive Value, % | Negative Predictive Value, % |
|---|---|---|---|---|
| ≥ 0.10 | 100 (100-100) | 0 (0-0) | 66.8 (63.7-69.9) | 100 (91.3-100) |
| ≥ 0.15 | 100 (99.7-100) | 0 (0-3.7) | 66.9 (63.8-70.0) | 100 (50.0-100) |
| ≥ 0.20 | 100 (99.2-100) | 1.0 (0-6.1) | 67.1 (64.1-70.5) | 88.9 (33.3-100) |
| ≥ 0.25 | 99.7 (98.8-100) | 3.3 (0-10.1) | 67.6 (64.5-70.9) | 83.3 (50.0-100) |
| ≥ 0.30 | 99.3 (97.7-100) | 5.6 (1.0-12.6) | 68.0 (64.9-71.3) | 80.0 (50.0-100) |
| ≥ 0.35 | 98.7 (96.3-99.7) | 9.2 (2.8-17.4) | 68.7 (65.5-71.9) | 76.9 (55.9-92.3) |
| ≥ 0.40 | 97.2 (93.5-99.4) | 13.6 (6.0-24.5) | 69.5 (66.4-72.8) | 71.0 (58.6-87.5) |
| ≥ 0.45 | 94.8 (88.6-98.1) | 20.0 (9.9-35.8) | 70.7 (67.4-74.0) | 65.3 (56.1-77.3) |
| ≥ 0.50 | 90.1 (83.8-95.7) | 29.8 (16.1-44.3) | 72.2 (69.1-75.8) | 60.2 (53.9-68.1) |
| ≥ 0.55 | 84.6 (79.2-91.6) | 39.9 (25.1-49.4) | 73.8 (70.4-77.3) | 56.3 (51.0-61.9) |
| ≥ 0.60 | 80.3 (75.2-85.8) | 45.8 (34.7-53.7) | 74.9 (71.7-78.1) | 53.5 (47.9-58.7) |
| ≥ 0.65 | 76.0 (65.7-81.4) | 51.5 (42.1-62.6) | 75.9 (72.7-79.3) | 51.1 (45.8-56.4) |
| ≥ 0.70 | 66.5 (45.3-77.8) | 61.8 (49.1-75.8) | 77.5 (74.2-81.0) | 47.6 (41.7-53.9) |
| ≥ 0.75 | 47.6 (23.1-67.6) | 76.0 (60.9-89.8) | 80.2 (76.4-84.6) | 41.6 (36.8-48.7) |
| ≥ 0.80 | 21.7 (0-48.5) | 91.4 (77.4-100) | 83.6 (70.4-90.9) | 36.3 (32.6-40.8) |
| ≥ 0.85 | 3.3 (0-12.8) | 98.6 (95.9-100) | 85.6 (67.9-95.6) | 33.9 (30.5-37.0) |
| ≥ 0.90 | 0 (0-5.2) | 100 (98.2-100) | 87.0 (72.1-98.1) | 33.3 (30.1-36.4) |

***Table 6 –*** *Predictive performance (median [95% confidence interval]) of organ-confined disease nomograms in 1000 validation bootstrap samples (nomogram-2).*

| Probability | Sensitivity, % | Specificity, % | Positive Predictive Value, % | Negative Predictive Value, % |
|---|---|---|---|---|
| ≥ 0.10 | 100 (100-100) | 0 (0-0) | 66.8 (63.9-69.8) | 100 (84.0-100) |
| ≥ 0.15 | 100 (99.7-100) | 0 (0-3.4) | 66.9 (63.9-69.8) | 100 (60.5-100) |
| ≥ 0.20 | 100 (99.1-100) | 0 (0-6.1) | 67.2 (64.2-70.1) | 88.2 (50.0-100) |
| ≥ 0.25 | 99.5 (98.7-100) | 3.3 (0-10.7) | 67.6 (64.6-70.6) | 80.0 (44.4-100) |
| ≥ 0.30 | 99.3 (98.1-100) | 5.6 (0-12.4) | 68.1 (65.2-71.1) | 80.0 (50.0-100) |
| ≥ 0.35 | 98.8 (96.1-99.8) | 9.1 (2.1-18.3) | 68.7 (65.7-71.6) | 77.2 (52.6-94.1) |
| ≥ 0.40 | 97.3 (94.0-99.5) | 13.0 (5.2-23.3) | 69.5 (66.5-72.6) | 71.1 (54.3-88.6) |
| ≥ 0.45 | 94.8 (88.7-98.8) | 19.4 (8.9-34.5) | 70.5 (67.7-73.8) | 64.9 (54.5-81.1) |
| ≥ 0.50 | 90.3 (83.5-95.8) | 28.9 (15.1-44.6) | 72.0 (69.0-75.8) | 59.7 (53.1-67.4) |
| ≥ 0.55 | 84.1 (79.0-91.9) | 40.2(24.0-49.8) | 73.8 (70.5-77.1) | 55.7 (50.3-61.5) |
| ≥ 0.60 | 79.9 (74.0-85.1) | 46.1 (36.0-54.4) | 74.9 (71.9-77.9) | 53.1 (47.7-58.1) |
| ≥ 0.65 | 75.7 (65.4-80.6) | 51.7 (43.5-63.7) | 76.0 (73.2-79.2) | 50.9 (45.7-56.0) |
| ≥ 0.70 | 66.6 (50.7-77.8) | 61.4 (49.3-73.1) | 77.6 (74.6-81.1) | 47.7 (42.4-53.4) |
| ≥ 0.75 | 48.5 (26.5-68.0) | 75.5 (61.4-89.2) | 80.2 (76.8-84.6) | 41.7 (36.9-48.7) |
| ≥ 0.80 | 23.5 (0-39.7) | 90.6 (82.5-100) | 83.7 (73.1-92.4) | 36.3 (32.6-41.2) |
| ≥ 0.85 | 3.2 (0-12.1) | 98.7 (95.7-100) | 86.6 (67.4-96.7) | 33.6 (30.8-37.0) |
| ≥ 0.90 | 0 (0-5.0) | 100 (98.2-100) | 86.7 (69.6-99.2) | 33.2 (30.2-36.3) |

sum of the two most prevalent glandular patterns that most frequently can be 3+4 or 4+3. Some studies have shown that the percentage of Gleason pattern 4 is related to extension and severity of the disease (31), motivating comparisons of these two scores. Chan et al. (34) found an organ-confined disease rate of 34.7% among patients with surgical Gleason score 7 that underwent radical prostatectomy. However, the risk of disease progression after surgery was 20% greater for patients with Gleason 4+3 when compared to patients with Gleason score 3+4 after 10 years follow up. It is important to point out that these results were based on analysis of the surgical specimens and not on biopsy samples as we discussed before (33). Conversely, Groeber et al. (35) did not find any difference between the groups with Gleason score 3+4 or 4+3 regarding extra-prostatic extension or seminal vesicle involvement.

In the present study we ratify the greater accuracy of the nomograms when compared to the analysis of a single prognostic variable. In patients with serum PSA between 0 to 4 ng/mL, the chance of an organ-confined disease was 78.6%, however, when considering biopsy Gleason score and PPBC, we found that the finding of an organ-confined disease can be observed in 70 to 86% of cases. Gancarczyk et al. (8), developed a nomogram based on the same variables and showed a 72% rate of an organ-confined disease when serum PSA was 4 ng/mL or lower. However, as shown in our series, when considering the biopsy Gleason score and PPBC, this rate varied from 54 to 80%. The same reasoning can be applied when considering biopsy Gleason score as a single variable that defines a 74.1% chance of an organ-confined disease in a patient with score 2 to 6. However, when all these three variables are considered together, we found that the same patient present a 51 to 86% chance of an organ confined disease. We also noted that patients with more than 75% positive biopsy cores have a 43.9% chance of presenting an organ-confined disease, the same number found by Gancarczyk et al. (8) considering a cut point of 60% for positive biopsy cores. However, this probability rises to 71% with favorable PSA levels and Gleason scores and reduces to 26% when both variables were unfavorable.

Finally, in the present study, we confirmed the superiority of the nomograms when compared to the analysis of a single prognostic factor. We emphasize that the PPBC is a very important parameter that should be incorporated in preoperative models, and that patients with biopsy Gleason score 7 can show the same disease extension when compared to patients with Gleason score 8 to 10.

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## CONFLICT OF INTEREST

None declared.

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