



Contemporary Update of Prostate Cancer Staging Nomograms or the New Millennium

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Introduction

The “Partin tables” were originally developed by urologists Alan W. Partin, M.D., Ph.D., and Patrick C. Walsh, M.D. based on accumulated data from hundreds of patients who had been treated for prostate cancer. Ingeniously correlating the three things that were known about a man's disease -- PSA level, Gleason score, and estimated clinical stage -- the tables were designed to help men and their doctors predict the definitive pathological stage (determined after surgery, when a pathologist examines the removed prostate for the presence of cancer) and best course of treatment. Now the tables have been updated to reflect the trends in presentation and pathologic stage for men newly diagnosed with clinically localized prostate cancer at James Buchanan Brady Urological Institute. Clinicians can use these nomograms to counsel individual patients and help them make important decisions regarding their disease.

Nomograms

Tables I to IV demonstrate the probability of presenting with the various pathologic stages when the preoperative serum PSA, biopsy Gleason histologic grade, and clinical stage (AJCC 1992) are known. The updated nomograms have modified PSA groups and Gleason sum groups. The PSA groups are divided into five categories: 0 to 2.5, 2.6 to 4.0, 4.1 to 6.0, 6.1 to 10, and more than 10.0 ng/mL to further sub stratify men with respect to their PSA level. Additionally, we sub stratified the Gleason scores into modified groups based on the risk of recurrence. In previous work from our institution, Kaplan-Meier actuarial survival curves (data not shown) for men with follow-up of more than 8 years demonstrated that biochemical progression free survival for tumours with Gleason score 2 to 4 were similar, as were those with a within-the-groups Gleason score of 5 to 6 and 8 to 10.⁷

Gleason Score is an assessment of the cancer aggressiveness, (a number from 2-10) taken by a pathologist from the tissue removed at the time of your radical prostatectomy.

PSA or prostate-specific antigen, is an enzyme made by the prostate, a highly sensitive measure of cancer recurrence; if the prostate is no longer in the body and PSA is being made at detectable levels, then some prostate cancer cells must remain in the body.

TNM Clinical Stage

T1a: Nonpalpable, with \leq 5% of tissue with cancer, low grade.(Diagnosed by TURP - Transurethral Resection of the Prostate)

T1b: Nonpalpable, with $>$ 5% of tissue with cancer and/or high grade(Diagnosed by TURP - Transurethral Resection of the Prostate)

T1c: Nonpalpable, but prostate-specific antigen elevated

T2a: Palpable, half of 1 lobe or less

T2b: Palpable, more than half of 1 lobe, not both lobes

T2c: Palpable, involves both lobes

T3a: Palpable, unilateral capsular penetration

Thus, these Gleason scores were sub grouped as 2 to 4, 5 to 6, or 8 to 10. Likewise, previous data have also demonstrated that Gleason sums of 3 +4=7 and 4 +3 =7 behave differently and warrant substratification.⁸

TABLE I. Clinical Stage T1c (nonpalpable, PSA elevated)						
PSA Range (ng/mL)	Pathologic Stage	Gleason Score				
		2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	Organ confined	95 (89-99)	90 (88-93)	79 (74-85)	71 (62-79)	66 (54-76)
	Extraprostatic extension	5 (1-11)	9 (7-12)	17 (13-23)	25 (18-34)	28 (20-38)
	Seminal vesicle (+)	—	0 (0-1)	2 (1-5)	2 (1-5)	4 (1-10)
	Lymph node (+)	—	—	1 (0-2)	1 (0-4)	1 (0-4)
2.6-4.0	Organ confined	92 (82-98)	84 (81-86)	68 (62-74)	58 (48-67)	52 (41-63)
	Extraprostatic extension	8 (2-18)	15 (13-18)	27 (22-33)	37 (29-46)	40 (31-50)
	Seminal vesicle (+)	—	1 (0-1)	4 (2-7)	4 (1-7)	6 (3-12)
	Lymph node (+)	—	—	1 (0-2)	1 (0-3)	1 (0-4)
4.1-6.0	Organ confined	90 (78-98)	80 (78-83)	63 (58-68)	52 (43-60)	46 (36-56)
	Extraprostatic extension	10 (2-22)	19 (16-21)	32 (27-36)	42 (35-50)	45 (36-54)
	Seminal vesicle (+)	—	1 (0-1)	3 (2-5)	3 (1-6)	5 (3-9)
	Lymph node (+)	—	0 (0-1)	2 (1-3)	3 (1-5)	3 (1-6)
6.1-10.0	Organ confined	87 (73-97)	75 (72-77)	54 (49-59)	43 (35-51)	37 (28-46)
	Extraprostatic extension	13 (3-27)	23 (21-25)	36 (32-40)	47 (40-54)	48 (39-57)
	Seminal vesicle (+)	—	2 (2-3)	8 (6-11)	8 (4-12)	13 (8-19)
	Lymph node (+)	—	0 (0-1)	2 (1-3)	2 (1-4)	3 (1-5)
>10.0	Organ confined	80 (61-95)	62 (58-64)	37 (32-42)	27 (21-34)	22 (16-30)
	Extraprostatic extension	20 (5-39)	33 (30-36)	43 (38-48)	51 (44-59)	50 (42-59)
	Seminal vesicle (+)	—	4 (3-5)	12 (9-17)	11 (6-17)	17 (10-25)
	Lymph node (+)	—	2 (1-3)	8 (5-11)	10 (5-17)	11 (5-18)

KEY: PSA = prostate-specific antigen.

TABLE III. Clinical Stage T2b (palpable > 1 .2 of one lobe, not on both lobes)						
PSA Range (ng/mL)	Pathologic Stage	Gleason Score				
		2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	Organ confined	88 (73-97)	75 (69-81)	54 (46-63)	43 (33-54)	37 (26-49)
	Extraprostatic extension	12 (3-27)	22 (17-28)	35 (28-43)	45 (35-56)	46 (35-58)
	Seminal vesicle (+)	—	2 (0-3)	6 (2-12)	5 (1-11)	9 (2-20)
	Lymph node (+)	—	1 (0-2)	4 (0-10)	6 (0-14)	6 (0-16)
2.6-4.0	Organ confined	80 (61-95)	63 (57-69)	41 (33-48)	30 (22-39)	25 (17-34)
	Extraprostatic extension	20 (5-39)	34 (28-40)	47 (40-55)	57 (47-67)	57 (46-68)
	Seminal vesicle (+)	—	2 (1-4)	9 (4-15)	7 (3-14)	12 (5-22)
	Lymph node (+)	—	1 (0-2)	3 (0-8)	4 (0-12)	5 (0-14)
4.1-6.0	Organ confined	75 (55-93)	57 (52-63)	35 (29-40)	25 (18-32)	21 (14-29)
	Extraprostatic extension	25 (7-45)	39 (33-44)	51 (44-57)	60 (50-68)	59 (49-69)
	Seminal vesicle (+)	—	2 (1-3)	7 (4-11)	5 (3-9)	9 (4-16)
	Lymph node (+)	—	2 (1-3)	7 (4-13)	10 (5-18)	10 (4-20)
6.1-10.0	Organ confined	69 (47-91)	49 (43-54)	26 (22-31)	19 (14-25)	15 (10-21)
	Extraprostatic extension	31 (9-53)	44 (39-49)	52 (46-58)	60 (52-68)	57 (48-67)
	Seminal vesicle (+)	—	5 (3-8)	16 (10-22)	13 (7-20)	19 (11-29)
	Lymph node (+)	—	2 (1-3)	6 (4-10)	8 (5-14)	8 (4-16)
>10.0	Organ confined	57 (35-86)	33 (28-38)	14 (11-17)	9 (6-13)	7 (4-10)
	Extraprostatic extension	43 (14-65)	52 (46-56)	47 (40-53)	50 (40-60)	46 (36-59)
	Seminal vesicle (+)	—	8 (5-11)	17 (12-24)	13 (8-21)	19 (12-29)
	Lymph node (+)	—	8 (5-12)	22 (15-30)	27 (16-39)	27 (14-40)

KEY: PSA = prostate-specific antigen.

TABLE IV. Clinical Stage T2c (palpable on both lobes)						
PSA Range (ng/mL)	Pathologic Stage	Gleason Score				
		2-4	5-6	3+4=7	4+3=7	8-10
0-2.5	Organ confined	86 (71-97)	73 (63-81)	51 (38-63)	39 (26-54)	34 (21-48)
	Extraprostatic extension	14 (3-29)	24 (17-33)	36 (26-48)	45 (32-59)	47 (33-61)
	Seminal vesicle (+)	—	1 (0-4)	5 (1-13)	5 (1-12)	8 (2-19)
	Lymph node (+)	—	1 (0-4)	6 (0-18)	9 (0-26)	10 (0-27)
2.6-4.0	Organ confined	78 (58-94)	61 (50-70)	38 (27-50)	27 (18-40)	23 (14-34)
	Extraprostatic extension	22 (6-42)	36 (27-45)	48 (37-59)	57 (44-70)	57 (44-70)
	Seminal vesicle (+)	—	2 (1-5)	8 (2-17)	6 (2-16)	10 (3-22)
	Lymph node (+)	—	1 (0-4)	5 (0-15)	7 (0-21)	8 (0-22)
4.1-6.0	Organ confined	73 (52-93)	55 (44-64)	31 (23-41)	21 (14-31)	18 (11-28)
	Extraprostatic extension	27 (7-48)	40 (32-50)	50 (40-60)	57 (43-68)	57 (43-70)
	Seminal vesicle (+)	—	2 (1-4)	6 (2-11)	4 (1-10)	7 (2-15)
	Lymph node (+)	—	3 (1-7)	12 (5-23)	16 (6-32)	16 (6-33)
6.1-10.0	Organ confined	67 (45-91)	46 (36-56)	24 (17-32)	16 (10-24)	13 (8-20)
	Extraprostatic extension	33 (9-55)	46 (37-55)	52 (42-61)	58 (46-69)	56 (43-69)
	Seminal vesicle (+)	—	5 (2-9)	13 (6-23)	11 (4-21)	16 (6-29)
	Lymph node (+)	—	3 (1-6)	10 (5-18)	13 (6-25)	13 (5-26)
>10.0	Organ confined	54 (32-85)	30 (21-38)	11 (7-17)	7 (4-12)	6 (3-10)
	Extraprostatic extension	46 (15-68)	51 (42-60)	42 (30-55)	43 (29-59)	41 (27-57)
	Seminal vesicle (+)	—	6 (2-12)	13 (6-24)	10 (3-20)	15 (5-28)
	Lymph node (+)	—	13 (6-22)	33 (18-49)	38 (20-58)	38 (20-59)

KEY: PSA = prostate-specific antigen.

Like our previous nomograms, PSA, Gleason score (biopsy), and clinical stage contributed significantly to the prediction of pathologic stage in the multinomial log-linear progression ($P < 0.001$). Also, as seen in our previous nomograms, similar results were seen when PSA was used as a continuous variable and all two-way and three-way interactions were tested and added little to the statistical significance of the final model ($P > 0.05$). The final model contained only the main effects, and the combination of the three variables predicted better than any single variable. The medians (95% confidence intervals [CIs]) of the predicted probabilities from the multinomial log-linear regression

analysis of 1000 bootstrap samples from the original study group are presented in the nomograms (Tables I to IV). The numbers within each cell of the nomogram represent the percentage of likelihood of a given pathologic stage based on the regression of all three variables combined. For example, a man with a preoperative serum PSA level of 2.7 ng/mL and a biopsy Gleason score of levels less than 10.0 ng/mL, and nonpalpable (Stage T1c) disease. This dramatic change in presentation, which may be due to PSA and better screening strategies, has nonetheless caused a major stage migration for prostate cancer, with nearly 60% of newly diagnosed cases presenting with localized or regional disease.¹ Our methods for predicting the pathologic stage, which were primarily developed from data collected from men treated before this stage migration,²⁻⁴ must also evolve to allow us to make accurate predictions for men newly diagnosed with prostate cancer. For this reason, we have updated our nomograms ("Partin Tables") to better represent the demographic, clinical, and biochemical data of men presenting with prostate cancer in 2001. Like our previous tables, simple, easily obtainable variables were used (serum PSA, biopsy Gleason score, and clinical stage [AJCC TNM-1992]) and combined into simple-to-use tables.

Several patients and physicians who used the previous nomograms² suggested that an individual with a serum PSA level of 4.1 ng/mL must have a higher probability of organ-confined disease than an individual with a PSA of 10.1 ng/mL with the same stage and Gleason score (e.g., T2c and 3 + 4 = 7). Intuitively, this seemed obvious; however, the previous tables "lumped" these men into the same group and provided limited differentiation with respect to the likelihood of the various pathologic stages. In the previous (1997) nomograms, both men would have had a likelihood of organ-confined disease of 25%; the new (2001) nomograms provide the first man with a likelihood of organ-confined disease of 31% (95% CI 23% to 41%). The second would have only an 11% (95% CI 7% to 17%) chance of organ-confined disease and no overlap in the confidence intervals. Additionally, two men with similar PSA levels (e.g., 5.2 ng/mL) and similar digital rectal examination results (e.g., T2a) might have a biopsy Gleason score of 3 + 4 = 7 (44% chance of organ-confined disease, 95% CI 39% to 50%) compared with a man with a biopsy Gleason score of 4 + 3 = 7 who has only a 33% chance of organ-confined disease, 95% CI 25% to 41% (little overlap in confidence intervals). The further stratification of the Gleason groups and the PSA groups are provided to better capture the actual probabilities of the various pathologic stages for the individual patient.

Since we presented our 1997 updated nomograms, investigators at the Mayo Clinic have independently evaluated this method of stage prediction on their cohort of patients and provided excellent validation of this method.⁹ Others have suggested the incorporation of race,¹⁰ biopsy information such as the number of cores or the percentage of cores involved,¹¹ or use of trans rectal ultrasound staging,¹² or nuclear chromatin texture characteristics¹³ into similar staging models. Although these suggestions may improve the prediction of the pathologic stage, they make the use of simple tables more cumbersome because of the increased number of variables and have yet to be validated in large cohorts of patients. Large numbers of variables (greater than three or four) will require the use of neural networks for stage prediction and are presently being evaluated for this purpose.¹⁴ Additionally, within this contemporary cohort, the numbers of biopsies with Gleason scores 2 to 4 are very limited and the probabilities should be interpreted with caution. At our institution, a Gleason score of 2 to 4 on prostate biopsy is no longer given.¹⁵ With only 6% African-American men in this cohort, the utility of these tables for African-American men is questionable. Within the only subgroup of African-American men with enough numbers for statistical analysis (T1c, 3+3=6, PSA 6.0 to 10.0 ng/mL, n = 38), the rate of organ-confined cancer was 81% for all men, 81% for white men, and 80% for African-American men. Thus, we continue to caution use of these tables for African-American men until they can be validated in other cohorts with larger numbers of African-American men.

The primary value of these updated “Partin Tables” will be for counselling patients regarding the probability of their tumour being a specific pathologic stage, rather than a strict decision-making tool. The nomograms may help patients and their treating physicians make informed decisions based on the probability of a pathologic stage, the individual patient's risk tolerance, and the values they place on the various potential outcomes. In addition, the use of these nomograms may aid in the rational selection of patients to undergo definitive therapy for prostate cancer with the hope of further improving the numbers and percentage of cancers that receive effective therapy that will cure the disease.

Conclusion

We have updated our nomograms for predicting pathologic stage for prostate cancer with a more contemporary cohort of men treated between 1994 and 2000. The new nomograms combine PSA, biopsy Gleason score, and clinical stage with improved sub stratification of both Gleason and PSA groups. The new “Partin Tables” may help us counsel our patients regarding their likelihood of having various pathologic stages and aid in important decision making.

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