Int J Clin Exp Pathol 2012;5(6):496-502
www.ijcep.com /ISSN:1936-2625/IJCEP1205005

Original Article

Predictors of Gleason Score (GS) upgrading on subsequent prostatectomy: a single Institution study in a cohort of patients with GS 6

Vikas Mehta[1], Kevin Rycyna[2], Bart MM Baesens[4], Güliz A Barkan[1], Gladell P Paner[1*], Robert C Flanigan[3], Eva M Wojcik[1], Girish Venkataraman[1]

Departments of [1]Pathology, [2]Stritch School of Medicine and [3]Urology, Loyola University Medical Center, Maywood, IL; [4]Department of Decision Sciences and Information Management, Catholic University Naamsestraat 69 3000 Leuven, Belgium. [*]Current affiliation: Department of Pathology, University of Chicago Hospital, Hyde Park, IL.

Received May 13, 2012; Accepted June 3, 2012; Epub July 29, 2012; Published August 15, 2012

Abstract: Background: Biopsy Gleason score (bGS) remains an important prognostic indicator for adverse outcomes in Prostate Cancer (PCA). In the light of recent studies purporting difference in prognostic outcomes for the subgroups of GS7 group (primary Gleason pattern 4 vs. 3), upgrading of a bGS of 6 to a GS≥7 has serious implications. We sought to identify pre-operative factors associated with upgrading in a cohort of GS6 patients who underwent prostatectomy. Design: We identified 281 cases of GS6 PCA on biopsy with subsequent prostatectomies. Using data on pre-operative variables (age, PSA, biopsy pathology parameters), logistic regression models (LRM) were developed to identify factors that could be used to predict upgrading to GS≥7 on subsequent prostatectomy. A decision tree (DT) was constructed. Results: 92 of 281 cases (32.7%) were upgraded on subsequent prostatectomy. LRM identified a model with two variables with statistically significant ability to predict upgrading, including pre-biopsy PSA (Odds Ratio 8.66; 2.03-37.49, 95% CI) and highest percentage of cancer at any single biopsy site (Odds Ratio 1.03, 1.01-1.05, 95% CI). This two-parameter model yielded an area under curve of 0.67. The decision tree was constructed using only 3 leave nodes; with a test set classification accuracy of 70%. Conclusions: A simplistic model using clinical and biopsy data is able to predict the likelihood of upgrading of GS with an acceptable level of certainty. External validation of these findings along with development of a nomogram will aid in better stratifying the cohort of low risk patients as based on the GS.

Keywords: Carcinoma, prostate/pathology/predictive modeling, statistical techniques/logistic regression, binary recursive partitioning

Introduction

Many recent studies have shown that the prostate cancers with Gleason score (GS) =7 have an adverse and varied prognosis depending on the primary Gleason pattern. Understandably, upgrading of a GS6 on a biopsy to a GS7 or more on prostatectomy may translate into potential adverse outcomes for the patient. King et al defined "clinically significant" upgrading of the biopsy as any of the following: (i) a biopsy Gleason score (bGS) of 6 to a prostatectomy GS (pGS) of 7 or higher, (ii) a bGS 3 + 4 to a pGS of 4 + 3 or higher, and (iii) a bGS of 7 to a pGS of 8 or higher [1]. The reported rates of clinically significant upgrading in recent studies are widely varying, ranging from 14% [2] to up to 71.7% [3]. Factors affecting upgrading rates have been influenced by the type of biopsy (sextant vs. Extended biopsy scheme) [4, 5], stage [6, 7], PSA [6-8], number of core biopsies [9] and biopsy GS [6, 7]. The goal of this study is to provide more clarification to this important discussion by identifying the clinical variables that correlated with upgrading from bGS of 6 to a pGS of 7 or more in this patient cohort at a tertiary care institution in the PSA era.

Material and methods

Case selection

The study population consisted of a cohort of patients who had a biopsy diagnosis of prostate cancer between 1998 and 2002 based on

Table 1. Baseline characteristics of this cohort of 281 patients with GS=6. Cochran-Armitage test was used to test the significance of linear trend of proportion of upgraded cases across the progressive quintiles of PSA.

Characteristics	Not upgraded (n=189)	Upgraded (n=92)	Significance
Age at testing median (range), y	58 (42-73)	58.5 (48-77)	0.21
Pre-biopsy PSA			**0.0001**
Quintile 1 (0.6-4.1 ng/mL)	47 (24.9%)	9 (9.8%)	
Quintile 2 (4.2-5 ng/mL)	41 (21.7%)	19 (20.7%)	
Quintile 3 (5.1-5.9 ng/mL)	39 (20.6%)	14 (15.2%)	
Quintile 4 (6-8.4 ng/mL)	35 (18.5%)	21 (22.8%)	
Quintile 5 (8.5-63.8 ng/mL)	27 (14.3%)	29 (31.5%)	
hPSA, median (range)	10 (1-80)	20 (2-10)	**0.001**
PPBS, median (range)	50 (17-100)	42.9 (17-100)	0.69
HGPIN in biopsy	21 (11.7%)	16 (19.3%)	0.09
PNI in biopsy	8 (4.4%)	3 (3.6%)	0.75

either digital rectal examination (DRE) or elevated PSA at screening. The study was conducted after full approval of the Loyola University Medical Center Institutional Review Board (LU 108763). The department of pathology database was searched for all radical prostatectomies conducted at the institution between 1998 and 2002 for a biopsy diagnosis of PCa from this group of patients. A total of 647 PCa patients diagnosed with concurrent prostatectomy data and biopsy data available were identified from this database. From this dataset, we selected a cohort of 281 patients with a biopsy GS6 that were diagnosed between 1998-2002. Most of these biopsies were from a pre-extended biopsy era and the median number of core biopsies was 8 (range = 6-12). The radical prostatectomy specimen was submitted entirely if the specimen weighed less than 50grams and every other section in case of specimens weighing more than 50 grams. Clinical data including age, pre-biopsy PSA, and biopsy variables including percentage of positive biopsy sites (PPBS), highest percentage of cancer at any single site with cancer (hPCA), and presence of high-grade prostatic intra-epithelial neoplasia (HGPIN) or perineural invasion (PNI) were extracted.

Statistical analyses

Cases with missing values on any of the aforementioned variables were deleted from the analyses. After appropriate transformation, Kolmogorov-Smirnov test for all scale data were not significant anymore. For univariate analyses, either Student's t-test or the non-parametric two independent sample test (Mann-Whitney's U test) was used for comparing differences in age, hPCA, PPBS and pre-biopsy PSA between the two outcome groups (upgraded vs. not upgraded). Multivariate logistic regression models (LRM) using a forward Wald method were constructed in Stata 10 (Statacorp, College Station, TX) to identify factors predictive of upgrading to GS>6. Odds Ratio (OR) and 95% confidence intervals (CI) of the OR were estimated and reported after exponentiation of the beta estimates. Receiver Operator Characteristic (ROC) curves were constructed and the area under curve (AUC) for the models was evaluated using the "c" statistic. Additionally, a decision tree (DT) was constructed using the Weka workbench using significant predictors from the LRM analyses to estimate cut-points and classification accuracy [10, 11].

Results

The baseline demographic information of the patients selected for the study is depicted in **Table 1**. There was no significant difference in age between the two groups of patients. Among 281 patients with GS=6, ninety-two (92) were upgraded to GS>6 (32.7%). Among the upgraded cases, 90 (97.8%) were upgraded to GS 7, and 1 each (1.1%) was upgraded to GS 8 and GS 9. Baseline univariate analyses revealed only pre-biopsy PSA and highest percentage of cancer at any single biopsy site to be statisti-

Table 2. Results of uni- and multi-variable analyses. Only log (PSA) and hPCA at a single biopsy site had the best ability to predict upgrading to a significant extent.

Predictor	Univariate Statistics		Multivariable Statistics	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age	1.02 (0.99, 1.06)	0.15	1.02 (0.97, 1.06)	0.319
PSA	12.36 (4.32, 39.24)	0.0001	8.04 (2.18, 21.65)	**0.002**
hpCA	1.02 (1.01, 1.03)	0.001	1.02 (1.01, 1.04)	**0.001**
PPBS	1.00 (0.99, 1.01)	0.533	0.99 (0.98, 1.01)	0.897
HGPIN	0.55 (0.27, 1.12)	0.102	0.47 (0.22, 1.02)	0.057
PNI	1.24 (0.32, 4.8)	0.755	3.6 (0.53, 24.33)	0.188

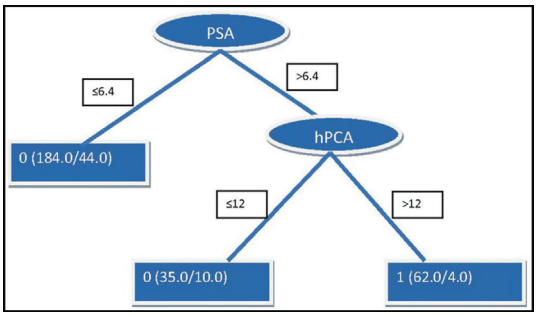

Figure 1. Decision tree analyses using prebiopsy PSA and hPCA. Binary cutpoints derived using this analyses are illustrated. The tree was constructed using 66% of the data for training and the remaining 34% for testing. Using only 3 leave nodes, the tree obtained a test set classification accuracy of 70%.

cally higher in cases that were upgraded (see **Table 2**).

LRM identified a model including both the significant variables from univariate analyses that had a statistically significant ability to predict upgrading, including pre-biopsy PSA (Odds Ratio 8.66; 2.03-37.49, 95% CI) and hPCA (Odds Ratio 1.03, 1.01-1.05, 95% CI). This two-parameter model yielded a predictive accuracy of 62.2% (AUC=0.67). None of the other variables (age, PPBS, or presence of HGPIN) were included in the final model. (**Table 2**) PNI was not included for modeling in the multivariable analyses owing to very few cases that had PNI in both outcome groups.

DT analysis (**Figure 1**) showed that the root node first splits on the PSA attribute, followed by a subsequent split on hPCA in the right branch. The tree was constructed using 66% of the data for training and the remaining 34% for testing. Using only 3 leave nodes, the tree obtained a test set classification accuracy of 70%. The corresponding ROC area was 60% (0.6). Hence, using only a few leave nodes, the tree was able to give satisfactory classification performance.

Discussion

While the incidence of PCA has been increasing over the past decade, a substantial downward trend in clinical stage and median PSA levels at diagnosis are being observed. Furthermore, there has also been a 3 fold decrease in the incidence of clinical stage T3 to T4 with increasing detection of low-volume cancer due to increased numbers of biopsies being performed [12]. Therefore, clinical stage and PSA level are becoming less relevant when classifying patients as low, intermediate, or high risk for treatment failure and disease progression. Gleason score, on the other hand, has been found to directly correlate with PSA failure, time to metastases and cancer specific mortality [13-15].

Although, prostatectomy Gleason score (pGS) is more accurate at predicting biochemical failure than biopsy Gleason score (bGS) [16]. However, it is the bGS that is available to the clinician and patient before a definitive treatment strategy is decided upon. Many studies have clearly shown significant discrepancies between bGS and pGS of the radical prostatectomy (RP) specimen. Furthermore, since low Volume/Low risk PCA is best served by RP, accurate identification of this subset on biopsy as GS6 or less is important since upgrading of a GS6 to a GS7 on RP may adversely change the risk levels and outcomes for this so called low-risk group as determined on a biopsy.

Table 3. Summary of major studies till date investigating the factors associated with upgrading.

Authors	Year	Biopsy Cohort Characteristics	Upgrading Rate (Criteria)	Predictive Factors	Notable Results
Dong *et al*	2008	268 GS6 patients	50%	PSA, prostate volume and biopsy cancer volume	Pts. With upgrading with shorter RFS
Kulkarni *et al*	2007	175 low-risk Pca	34%	PSA, Path Expertise	Nomogram with c=0.71 (BCA*=0.65)
Pinthus et al.	2006	Subset of 205 with GS6	~50%	PSA, Tumor volume on Biopsy	
Mian et al	2006	426 patients (225 Sextant; 206 EB**)	44%	Type of Biopsy (EB vs.Sextant)	Extended Biopsy scheme with less upgrading
King et al	2006	371 patients	40.70%	None	Independent of Tumor volume or clinical indices
Chun et al	2006	4789 patients with GS 6 and GS7	28.2% (King et al's criteria)	PSA, Clin. stage, bGS	BCA=0.75
Chun et al	2006	2880 patients with GS<=6	36.7% (King et al's criteria)	PSA, Clinical stage, bGS	Nomogram with BCA=0.804
King et al	2005	Subset of 72 patients with GS=6	32%	None	Volume indices do not predict upgrading
D'Amico et al	1999	420 Clinical T1c with bGS<=6	40%	PSA, prostate volume, Clin. stage 2b, 2c	

**BCA = Bootstrap Corrected Accuracy; **EB = Extended Biopsy. For studies since 2008 please see discussion.*

The reported incidence of upgrading is very varied in literature depending on the definition used and the type of biopsy schema (extended vs. sextant) [1, 4, 5]. The term "clinically significant upgrade" was coined by King et al, and refers to either a bGS of 6 upgraded to a pGS of 7 or higher, a bGS of 3+4 upgraded to a pGS of 4+3 or higher, or a bGS of 7 upgraded to pGS of 8 or higher [2]. This upgrading is important due to the implications on treatment options indicated for a Gleason score of ≤6, 7, or ≥8. Of note, cancers with a bGS of 6 that were upgraded to pGS of 7 matched the pathologic characteristics of cancers with a bGS of 7 and pGS of 7. These characteristics included cancer volume, margin and seminal vesicle status, capsular involvement, and extraprostatic extension. Patients who had a bGS of 6 and remained pGS of 6 had significantly better pathologic characteristics. These three scenarios demonstrate the overall significance of the final pathologic GS compared to the bGS.

Many recent studies have investigated the factors that predict upgrading. A summary of the major recent studies is depicted in **Table 3**. One of the early studies by D'Amico et al identified that higher baseline PSA and clinical stage are significantly associated with upgrading [6]. The predictive value of PSA for upgrading has been reaffirmed in many subsequent studies [3, 4, 17]. However the utility of clinical stage was questionable in other subsequent studies [1, 5, 18]. Recent studies have determined that the prostate specific antigen density or percentage free PSA are significant independent predictors of Gleason upgrading even when accounting for prostate specific antigen [19-21]. Men with a higher PSA level, perineural invasion and high-volume cancer at biopsy are most likely to be upgraded, while men with a large prostate volume and low-volume cancer at biopsy are more likely to be downgraded [22]. The reported rates of upgrading are varied in literature ranging from 14% in the cohort of King et al [2] to 71.1% in the study by Cam et al [3]. We included the cohort of GS6 patients in our study and PSA remained an independent predictor of Gleason upgrading in our study too, in agreement with most previous studies. In addition, the highest percentage of cancer was an additional significant predictor in our study. Interestingly, the import of tumor volume on Gleason upgrading has been conflicting in past

literature with some reporting significant utility [18], while other studies have failed to demonstrate its utility [13, 23]. Notably, the latter study concluded that histologic grading from small amounts of cancer in prostate biopsies is reliable and not more prone to grading errors. These authors advocate that a repeat biopsy for these patients may not be indicated.

There are two proposed reasons for the varied incidence of clinically significant upgrading, one involving interpretational bias and the other citing sampling effects due to tumor heterogeneity. However, there is disagreement within the literature as to whether an extended biopsy scheme could lower the incidence of significant upgrading compared to the standard sextant biopsy pattern. Capitanio and coworkers found that in men assessed with 10-12 cores, the rate of GSU was 47.9% compared with 23.5% if >18 cores were taken [9]. Currently, the focus has moved towards using clinical factors to predict the probability of significant GS upgrading between biopsy and RP. The accuracy of the models from recent major studies have ranged between 65 [24]-81% [7]. Notably, Kulkarni et al [16] developed a nomogram with an accuracy of 0.71 and their nomogram included PSA, which was a significant predictive factor. Similarly Moussa et al [25] developed a nomogram that had a concordance index of 0.68. Their cohort is similar to ours in that both included GS6 patients.

Nonetheless, there are some limitations to our study that merit addressing: first, we included solely patients with subsequent RP data available. Hence, it is not possible for us to estimate with certainty if the similar low-risk patients who do not undergo RP would have potential high-risk disease. Second, most patients underwent RP around a median duration of 2 months after biopsy and so it is unclear how much the disease characteristics may change in this interval. Thirdly the number of core biopsies taken in our cohort of patients is less (range 6-12) compared to more recent prostate biopsy protocols where up to 18 cores are submitted for pathological evaluation. However, at the same time there are studies in the literature that have shown that the number of core biopsies obtained is significantly lower in Gleason score upgraded patients in comparison to unchanged/downgraded Gleason score group. Also the prostate biopsy protocols are still heterogeneous and reflecting current daily urological practice with usage of nomograms based on six- and eight-core biopsy schemes [26]. Nonetheless, the efficacy of our model is comparable to the model developed by Kulkarni et al [24] with similar rates of upgrading. An important caveat for potential investigators regarding our study is that the applicability of our model may only be valid in cohorts with similar proportions of upgraded cases. Lastly, our sample size was insufficient to lend itself to a split-sample validation; keeping this in mind, we have performed a bootstrap validation to confirm our findings (not shown).

Since the variance in upgrading status is only partly explained by model, other factors may still contribute to upgrading including clinical stage, which we have not included in our study. Nonetheless, we have a chosen a surrogate of tumor volume (hPCA) that is fast easily reproducible, and accurate for pathologists to estimate at the time of report sign out, instead of cumbersome indices as millimeter lengths of cancer, overall percentage of cancer etc. Hence, our aim was also to develop a model that could easily be used in a nomogram at the time of sign-out. If our data is validated in an external cohort from a western population, then such nomogram information may even be incorporated as an addendum in pathology reports of all patients with a bGS of 6.

In conclusion, we report an upgrading rate of 32.7% in the GS6 cohort of patients who underwent subsequent RP. Pre-biopsy PSA and highest percentage of cancer in the biopsy are significant predictors of upgrading in the uni- as well as multivariable models. This information can be used as an adjunctive piece of informed clinical decision making when deciding potential treatment options for patients afflicted with low-risk prostate cancer, especially in patients seeking less invasive therapies such as active surveillance.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Address correspondence to: Girish Venkataraman, Department of Pathology, Loyola University Medical Center, Building 110, Room 2222, 2160 South First Avenue, Maywood, IL 60153 Phone: (708) 216-2053; Fax: (708) 327-2620; Email: gvenkat@lumc.edu

References

[1] King CR, McNeal JE, Gill H and Presti JC, Jr. Extended prostate biopsy scheme improves reliability of Gleason grading: implications for radiotherapy patients. International journal of radiation oncology, biology, physics 2004; 59: 386-391.

[2] King CR. Patterns of prostate cancer biopsy grading: trends and clinical implications. International journal of cancer. Journal international du cancer 2000; 90: 305-311.

[3] Cam K, Yucel S, Turkeri L and Akdas A. Accuracy of transrectal ultrasound guided prostate biopsy: histopathological correlation to matched prostatectomy specimens. International journal of urology : official journal of the Japanese Urological Association 2002; 9: 257-260.

[4] King CR and Long JP. Prostate biopsy grading errors: a sampling problem? International journal of cancer. Journal international du cancer 2000; 90: 326-330.

[5] Mian BM, Lehr DJ, Moore CK, Fisher HA, Kaufman RP, Jr, Ross JS, Jennings TA and Nazeer T. Role of prostate biopsy schemes in accurate prediction of Gleason scores. Urology 2006; 67: 379-383.

[6] Chun FK, Briganti A, Shariat SF, Graefen M, Montorsi F, Erbersdobler A, Steuber T, Salonia A, Currlin E, Scattoni V, Friedrich MG, Schlomm T, Haese A, Michl U, Colombo R, Heinzer H, Valiquette L, Rigatti P, Roehrborn CG, Huland H and Karakiewicz PI. Significant upgrading affects a third of men diagnosed with prostate cancer: predictive nomogram and internal validation. BJU international 2006; 98: 329-334.

[7] Chun FK, Steuber T, Erbersdobler A, Currlin E, Walz J, Schlomm T, Haese A, Heinzer H, McCormack M, Huland H, Graefen M and Karakiewicz PI. Development and internal validation of a nomogram predicting the probability of prostate cancer Gleason sum upgrading between biopsy and radical prostatectomy pathology. European urology 2006; 49: 820-826.

[8] D'Amico AV, Renshaw AA, Arsenault L, Schultz D and Richie JP. Clinical predictors of upgrading to Gleason grade 4 or 5 disease at radical prostatectomy: potential implications for patient selection for radiation and androgen suppression therapy. International journal of radiation oncology, biology, physics 1999; 45: 841-846.

[9] Capitanio U, Karakiewicz PI, Valiquette L, Perrotte P, Jeldres C, Briganti A, Gallina A, Suardi N, Cestari A, Guazzoni G, Salonia A and Montorsi F. Biopsy core number represents one of foremost predictors of clinically significant gleason sum upgrading in patients with low-risk prostate cancer. Urology 2009; 73: 1087-1091.

[10] Ian H, Witten EF. Data Mining: Practical Machine Learning Tools and Techniques. San Fransisco: Morgan Kaufmann 2005.

[11] Quinlan JR. C4.5: Programs for Machine Learning. San Mateo: Morgan Kaufmann 1993.

[12] Cooperberg MR, Lubeck DP, Mehta SS and Carroll PR. Time trends in clinical risk stratification for prostate cancer: implications for outcomes (data from CaPSURE). The Journal of urology 2003; 170: S21-25; discussion S26-27.

[13] Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD and Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. JAMA : the journal of the American Medical Association 1999; 281: 1591-1597.

[14] Freedland SJ, Humphreys EB, Mangold LA, Eisenberger M, Dorey FJ, Walsh PC and Partin AW. Risk of prostate cancer-specific mortality following biochemical recurrence after radical prostatectomy. JAMA : the journal of the American Medical Association 2005; 294: 433-439.

[15] D'Amico AV, Whittington R, Malkowicz SB, Wu YH, Chen MH, Hurwitz M, Kantoff PW, Tomaszewski JE, Renshaw AA, Wein A and Richie JP. Utilizing predictions of early prostate-specific antigen failure to optimize patient selection for adjuvant systemic therapy trials. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 2000; 18: 3240-3246.

[16] D'Amico AV, Whittington R, Malkowicz SB, Schultz D, Schnall M, Tomaszewski JE and Wein A. A multivariate analysis of clinical and pathological factors that predict for prostate specific antigen failure after radical prostatectomy for prostate cancer. The Journal of urology 1995; 154: 131-138.

[17] Pinthus JH, Witkos M, Fleshner NE, Sweet J, Evans A, Jewett MA, Krahn M, Alibhai S and Trachtenberg J. Prostate cancers scored as Gleason 6 on prostate biopsy are frequently Gleason 7 tumors at radical prostatectomy: implication on outcome. The Journal of urology 2006; 176: 979-984; discussion 984.

[18] King CR, McNeal JE, Gill H, Brooks JD, Srinivas S and Presti JC, Jr. Reliability of small amounts of cancer in prostate biopsies to reveal pathologic grade. Urology 2006; 67: 1229-1234.

[19] Magheli A, Hinz S, Hege C, Stephan C, Jung K, Miller K and Lein M. Prostate specific antigen density to predict prostate cancer upgrading in a contemporary radical prostatectomy series: a single center experience. The Journal of urology 2010; 183: 126-131.

[20] Visapaa H, Hotakainen K, Lundin J, Ala-Opas M and Stenman UH. The proportion of free PSA and upgrading of biopsy Gleason score after radical prostatectomy. Urologia internationalis 2010; 84: 378-381.

[21] Tilki D, Schlenker B, John M, Buchner A, Stanislaus P, Gratzke C, Karl A, Tan GY, Ergun S, Tewari AK, Stief CG, Seitz M and Reich O. Clinical and pathologic predictors of Gleason sum upgrading in patients after radical prostatectomy: results from a single institution series. Urologic oncology 2011; 29: 508-514.

[22] Moussa AS, Kattan MW, Berglund R, Yu C, Fareed K and Jones JS. A nomogram for predicting upgrading in patients with low- and intermediate-grade prostate cancer in the era of extended prostate sampling. BJU international 2010; 105: 352-358.

[23] King CR, Patel DA and Terris MK. Prostate biopsy volume indices do not predict for significant Gleason upgrading. American journal of clinical oncology 2005; 28: 125-129.

[24] Kulkarni GS, Lockwood G, Evans A, Toi A, Trachtenberg J, Jewett MA, Finelli A and Fleshner NE. Clinical predictors of Gleason score upgrading: implications for patients considering watchful waiting, active surveillance, or brachytherapy. Cancer 2007; 109: 2432-2438.

[25] Moussa AS, Li J, Soriano M, Klein EA, Dong F and Jones JS. Prostate biopsy clinical and pathological variables that predict significant grading changes in patients with intermediate and high grade prostate cancer. BJU international 2009; 103: 43-48.

[26] Thomas C, Pfirrmann K, Pieles F, Bogumil A, Gillitzer R, Wiesner C, Thuroff JW and Melchior SW. Predictors for clinically relevant Gleason score upgrade in patients undergoing radical prostatectomy. BJU international 2012; 109: 214-219.