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PSA DENSITY IS A STRONGER PROGNOSTIC FACTOR THAN PSA FOR ADVERSE FINAL HISTOPATHOLOGIC OUTCOMES AND BIOCHEMICAL PROGRESSION FREE SURVIVAL IN CT3A PROSTATE CANCER

Joniau S., Hsu C.Y., Van Poppel H.

University Hospital Leuven, Dept. of Urology, Leuven, Belgium

Introduction & Objectives: We were interested in factors that allow the best PRE-treatment prognostic information in patients with clinically locally advanced prostate cancer (cT3a). Those are preoperative serum PSA, biopsy Gleason score (bGS) and PSA density (PSAD). The combination of PSA and bGS provides accurate predictions of final histopathology. Nevertheless, PSA and bGS are poor predictors of biochemical progression free survival (BPFS). The objective of this study is to determine whether PSAD is a stronger predictive factor than preoperative PSA for adverse final histopathology (positive section margins, seminal vesicle invasion and positive lymph nodes) and BPFS in cT3a prostate cancer.

Material & Methods: Between 1987 and 2004, 200 patients with unilateral cT3a prostate cancer, assessed by digital rectal examination, underwent RP and bilateral lymphadenectomy at our institution. The preoperative serum PSA, PSAD and bGS of each patient were recorded. Outcome variables were margin status, seminal vesicle invasion, nodal status and BPFS. Logistic regression and Cox proportional hazard analysis were used to analyze differences between the predictive values of PSAD and PSA, corrected for bGS.

Results: The mean age was 63.3 years (range 41-79), mean follow-up was 70.6 months (range 7-77). The mean PSAD was 0.37 (range 0.03-1.77), mean PSA was 14.9 (range1.0-127.0), mean bGS was 6.6 (range 2-10). Sixty-seven patients had positive margin, 32 had seminal vesicle invasion and 17 had lymph node invasion. BPFS was 59.5% at 5 years and 51.1% at 10 years. In both uni-and multivariate logistic regression analysis and Cox analysis, PSAD proved to be an independent, highly significant and stronger predictor than PSA and bGS in all outcome variables. Logistic regression analysis

	Univariate				Multivariate			
		HR	95%CI	p		HR	95%CI	p
Margin	PSAD	8.73	2.93-26.06	<0.01	PSAD bGS	8.82	2.92-26.61	<0.01
	PSA	1.04	1.02-1.07	<0.01		1.15	0.89-1.48	0.27
	bGS	1.15	0.91-1.47	0.24	PSA bGS	1.04	1.02-1.07	<0.01
						1.17	0.91-1.50	0.22
Node	PSAD	6.22	1.83-21.19	<0.01	PSAD bGS	5.95	1.74-20.43	<0.01
	PSA	1.02	0.99-1.05	0.08		1.29	0.83-2.00	0.25
	bGS	1.32	0.86-2.03	0.20	PSA bGS	1.02	0.99-1-05	0.08
						1.33	086-2.05	0.20
SVI	PSAD	10.94	3.57-33.52	<0.01	PSAD bGS	11.55	3.63-36.79	<0.01
	PSA	1.07	1.04-1.11	<0.01		1.43	1.03-1.98	0.03
	bGS	1.41	1.03-1.92	0.03	PSA bGS	1.08	1.04-1.12	<0.01
						1.51	1.07-2.12	0.02

Cox regression analysis

	Univariate				Multivariate			
		HR	95%CI	p		HR	95%CI	p
BPFS	PSAD	3.91	2.14-7.12	<0.01	PSAD bGS	3.87	2.12-7.07	<0.01
	PSA	1.02	1.01-1.03	<0.01		1.03	0.86-1.23	0.74
	bGS	1.05	0.88-1.26	0.19	PSA bGS	1.02	1.01-1.03	<0.01
						1.05	0.87-1.26	0.62

Conclusions: PSAD is an independent prognostic factor, and is stronger than PSA, in the prediction of adverse histopathology and BPFS in cT3a prostate cancer. It can be used for patient counselling prior to treatment selection in locally advanced prostate cancer.

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THE PROGNOSTIC ROLE OF PREOPERATIVE CHROMOGRANIN A IN CLINICALLY LOCALISED PROSTATE CANCER TREATED WITH RADICAL PROSTATECTOMY

Masieri L.[1], Gontero P.[2], Serni S.[1], Marchioro G.[3], Mantella A.[1], Lanciotti M.[1], Zaramella S.[3], Minervini A.[1], Carini M.[1]

[1]University of Florence, Careggi Hospital, Dept. of Urology, Florence, Italy, [2]University of Turin, Dept. of Urology, Turin, Italy, [3]University of Piemonte Orientale, Dept. of Urology, Novara, Italy

Introduction & Objectives: The aim of the present study was to analyze the prognostic values of preoperative CgA as a marker of poor prognosis and recurrence after radical prostatectomy. Moreover we attempted to find a correlation with well known prognostic variables.

Material & Methods: This study comprises 306 patients with clinically localized prostate cancer prospectively recruited who underwent radical prostatectomy from January 2000 to May 2005. A blood sample for the determination of serum preoperative Chromogranine A value (radioimmuno assay CGA-RIACT) was obtained in all cases. All radical prostatectomy specimens were formalin fixed, coated with India ink, weighed and serially perpendicular sectioned, staged according to the 2002 American Joint Committee on Cancer (AJCC) staging system. Spearman correlation test was used to compare CgA values and other continuous variables. Kruskal-wallis test was used to analyze CgA levels differences among 3 or more groups of patients (PSA, GS, Stage), while the Mann Whitney test was used for 2 grouping variables (status). The probability of survival was estimated by the Kaplan-Meier method, with the log-rank test used to estimate differences among levels of the analyzed variables.

Results: Median (mean, 25%,75% percentile) CgA level for the 306 patients included was 68 ng/ml (100.1, 47.9-98.7). Correlation between age and CgA levels was positive and statistically significant (p<0.001). Moreover, patients were divided in two groups based on the median age (<68 and ≥68 years). The difference was statistically significant (p=0.002). The comparison of preoperative CgA values among patients grouped according to pathological stage (pT2, pT3a, pT3b, pT4, N+), Gleason score (GS 2-6, 7, 8-10) and preoperative PSA (< 10ng/ml, 10-20 ng/ml, > 20 ng/ml) did not achieve statistically significant differences. The mean (median, range) follow up was 21.18 months (18, 1-55 months). Of the 281 patients included in the survival analysis, 208 (74%) were free from biochemical recurrence (NED) and 73 (26%) presented a biochemical recurrence (PROG). The difference between CgA levels among NED and PROG patients was not statistically significant. Patient were stratified on the bases of the normal value of CgA (123ng/ml) and then according to the cut-off value of 68 ng/ml, but these were both unable to achieve significant risk stratification.

Conclusions: Studies on a possible prognostic role in localized hormone naïve prostate cancer have provided conflicting results. In our study population, larger than those published to date, we found a significant positive correlation of serum CgA with age, but no significant statistical correlation with other available variables and progression free survival. A possible explanation of our results could be that NE cells are not enough to raise circulating levels of CgA when dosed inpatients with localized prostate cancers.

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PREDICTION OF UNI OR BILATERAL PROSTATE CANCER GLAND'S INVOLVEMENT. IMPLICATIONS FOR NEURO-VASCULAR BUNDLES PRESERVATION

Raventos C.X.[1], Orsola A.[1], Cecchini L.L.[1], Planas J.[1], Trilla E.[1], De Torres I.[2], Morote J.[1]

[1]Hospital Vall d'Hebron, Dept. of Urology, Barcelona, Spain, [2]Hospital Vall d'Hebron, Dept. of Pathology, Barcelona, Spain

Introduction & Objectives: Patients with clinically organ confined prostate cancer frequently undergo a radical prostatectomy. Cancer distribution on the gland could determine the surgical management of the neurovascular bundles (NVB). The preoperative knowledge of the uni or bilateral gland's involvement may be useful for NVB preservation. The objective of this study is to know which clinical and biopsy pathological variables can predict uni/bilateral cancer extension on the gland.

Material & Methods: We analysed 274 patients who underwent radical prostatectomy. According to cancer gland's extension on the radical prostatectomy specimen, patients were divided into two groups: one lobe involvement (44,2%) and bilateral disease (55,8%). Clinical variables and parameters based on biopsy were studied as predictors of uni or bilateral extension of prostate cancer and analyzed on multiple logistic regression. Cut-offs of the predictive variables were selected. Besides, correlation between uni/bilateral cancer extension on the gland and prostate cancer burden was studied.

Results: The following variables were significantly different between both groups: prostate volume, biopsy Gleason interval (<=6 vs. >=7), number of positive cylinders (NPC), percentage of positive cylinders (%PC) and uni-bilaterality of biopsy positive cores. Total PSA, percentage of most affected cylinder and peri-neural invasion did not significantly differ. On multiple logistic regression, prostate volume (p 0,026) and interval of biopsy Gleason (p 0,016) raised as independent predictors of uni-bilaterality on the specimen. Of note, 50% of unilateral positive biopsy cases had bilateral extension on the gland. This bilateral involvement of the specimen was significantly associated to larger and multifocal tumours. Regarding bilateral involvement, using a prostate volume threshold of <=30cc and biopsy Gleason score >=7 we obtained 84% specificity and VPP 68%. On the other hand, using a prostate volume threshold of >=60cc and biopsy Gleason score <=6 we obtain 94% specificity and VPP 70% for unilateral extension.

Conclusions: Unilateral positive biopsy does not predict one lobe involvement and should not be used as a criteria for NVB preservation. Instead, both prostate volume and biopsy Gleason score might be useful to address NVB preservation. Small glands with biopsy gleason >=7 will more probably present bilateral cancer extension while larger glands with biopsy gleason <=6 will more probably have only one lobe involved and might benefit for NVB preservation.

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IS THERE A DIFFERENCE IN SUPERSENSITIVE PSA (SPSA) LEVEL WITH THE SITE OF POSITIVE MARGIN POST RADICAL PROSTATECTOMY?

Vaidyanathan R.[1], Rao A.[1], Motiwala H.[1], Laniado M.[1], Brown R.S.D.[2], Karim O.[1]

[1]Wexham Park Hospital, Dept. of Urology, Slough, United Kingdom, [2]Wexham Park Hospital, Dept. of Clinical Oncology, Slough, United Kingdom

Introduction & Objectives: The apex is a common site for a positive margin post radical prostatectomy. A positive apical margin is, however, not invariably associated with residual cancer. We have tried to determine whether sPSA is different in organ and specimen confined disease compared to a positive apical or other surgical margin in prostate cancer.

Material & Methods: 159 consecutive radical prostatectomy patients, followed for a minimum of 12 months, were studied retrospectively. Patients were grouped according to pathological stage and sPSA nadir was determined 6 weeks post surgery.

Results: 63 patients were Margin Positive +ve. sPSA nadir was similar in Apex +ve patients compared to those with Organ / Specimen confined disease. sPSA was significantly greater in the remaining Margin +ve patients.

Histology Group	Number	sPSA nadir (mg/L)	*P value
Organ / Specimen confined	96	0.012 ± 0.02	
Margin Positive (+ve)			
Apex +ve	18	0.015 ± 0.01	0.24
Other margin +ve	45	0.202 ± 0.5	0.03

*p value by student t test. ± Standard Deviation.

Conclusions: These data indicate that post-operative sPSA level is significantly lower in apex positive margin prostate cancer compared to other margins. This finding is consistent with the observation that a positive apical margin does not invariably indicate residual cancer