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Pathology

A Correlation Study on Serum Prostate Specific Antigen Levels and Gleason Grading In Transrectal Ultrasound Guided Prostatic Biopsies- A Tertiary Care Hospital Experience

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Abstract **Original Research Article**

Prostate Specific Antigen is considered as an established tumor marker in diagnosis, staging and evaluation of prostatic adenocarcinoma. However the utility of serum PSA alone in the interpretation of prostate carcinoma remains controversial and uncertain since it lacks sensitivity and specificity. Gleason score and grade grouping determines the biological behavior and acts as important parameters in staging and prognosis of prostatic carcinoma. Hence in our study we aimed to correlate the serum PSA levels with gleason score and grade group in the diagnosis and evaluation of prostatic adenocarcinoma in Transrectal ultrasound guided prostatic biopsies. The study was conducted in a tertiary care hospital, South India over a period of one year (2018-2019). We evaluated a total of 36 TRUS guided prostatic core biopsies. We found that the percentage of positivity for adenocarcinoma is about 50% of the total cases. The mean PSA value was 3.83(±5.43) in benign cases and 80.39(±99.07) in malignant cases. Serum PSA levels were higher in biopsies with high gleason scores and grade. The diagnostic efficacy of serum PSA level was significant with an area under the ROC curve of 0.972 which showed high sensitivity and specificity.

Keywords: Prostate Specific Antigen (PSA), Prostatic adenocarcinoma, Gleason score, Gleason grading, Sensitivity.

INTRODUCTION

Prostate carcinoma is considered as the second most common malignancy in men [1, 2]. The incidence and mortality rates of prostate cancer are age specific [1, 2]. Prostate specific antigen is a glycoprotein enzyme secreted by the epithelial cells of the prostate gland [3]. The diagnosis of prostate cancer are based on elevated serum prostate specific antigen levels and digital rectal examination clinically [3]. Studies reveal that for routine screening PSA levels are utilized to detect asymptomatic and early stages of prostate carcinoma but studies have found no significant impact in overall reduction of mortality rate[3,4]. Recent studies has shown that about 15% of men with normal PSA values have prostate cancer and nearly 2% would have higher grade of malignancy [4]. Also in most of the cases patients with raised PSA levels turn out not to have prostate cancer when a biopsy is done which may provide false assurance to the patients [5]. Current studies recommend TRUS guided imaging prostatic biopsies in suspected cases along with digital rectal examination [5]. In our study we analysed 36 TRUS guided prostatic core biopsies from patients with suspected prostatic pathology and correlated Serum PSA levels with the corresponding histopathological gleason score and grade group .

MATERIALS AND METHODS

The study was conducted over a period of one year (2018-2019) in the histopathology department of a tertiary care hospital.The core biopsies were taken using transrectal ultrasound guided imaging from clinically suspected lesions during digital rectal examination in the department of urology from the same hospital. The cases for which preoperative serum PSA levels are not recorded were excluded from our study. We evaluated a total of 36 TRUS guided prostatic core biopsies received with known serum PSA levels .Prostatic core biopsies from different areas of prostate were received in formalin which were labelled and sent in separate vials. The individual linear cores were measured and embedded for detailed study. For each of the paraffin embedded blocks the tissue sections was taken at several levels with maximum thickness of 4µm. The sections taken in the slide were stained with hematoxylin and eosin staining method. The College of

American pathologists protocol 2018 was applied to the diagnosed cases of prostatic adenocarcinoma. A Modified ISUP Gleason scoring criteria (2015) and grade grouping recommended by AJCC was used in these cases. Descriptive analysis and hypothesis testing was done by appropriate statistical tests by commercially available statistical software packages. (Unpaired t-Test) All quantitative variables were estimated using measures of central location (i.e) Mean and Standard deviation. A Receiver operating characteristic curve was plotted for representing the sensitivity and specificity of serum PSA levels.

RESULTS

Table-1: Comparison of Age in Benign and Malignant group

Disease Group	AGE (Mean ± SD)	p-value
Benign(N=18)	70.17±7.79	0.468
Malignant(N=18)	68.22±8.12	

Table-2: Comparison of PSA value and Gleason scores in Benign and Malignant group

Disease Group	Mean PSA (±SD)ng/ml	p-value
Benign	3.83±5.43	0.002*
Malignant	80.39±99.07	

*Statistically significant at the level of 0.05(p<0.05)

Table-3: Distribution of malignant cases according to Gleason score and grade grouping

Gleason Score	Grade grouping	Number of cases (%)
6(3+3)	1	1 (2.8)
7(4+3)	2	5 (13.9)
8(4+4)	4	2 (5.6)
9(5+4)	5	9 (25.0)
10(5+5)	5	1 (2.8)

Table-4: Comparison of Serum PSA value between high risk and low to intermediate risk groups

Gleason score	Number of cases	Serum PSA Mean±SD	P-value
Low to intermediate (Gleason score <8)	06	16.46±36.33	0.036*
High (Gleason score >=8)	12	108.80±118.09	

*Statistically significant at the level of 0.05(p<0.05)

Table-5: Diagnostic efficacy of serum PSA levels

Area	Std. Error[a]	p-value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.972	0.024	0.000	0.924	1.000

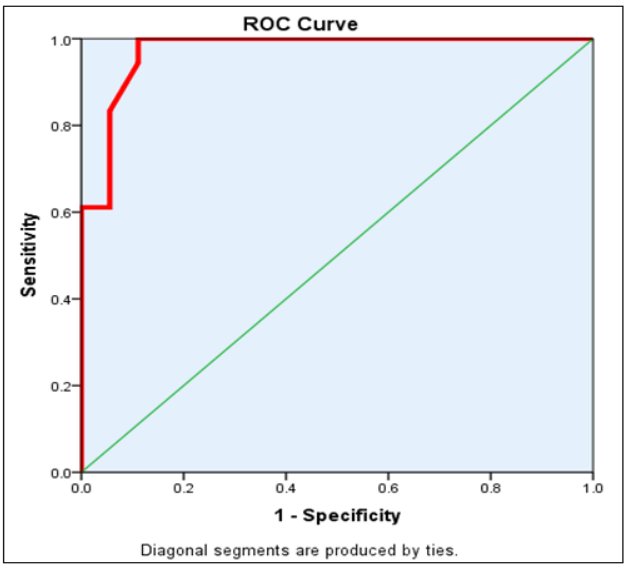

Fig-1: ROC Curve of Serum PSA levels

Table-6: Optimal cut off value of Serum PSA level to segregate malignant and benign cases

Positive if Greater Than or Equal To[a]	Sensitivity	1 –Specificity
0.00	1.000	1.000
1.50	1.000	.778
2.50	1.000	.444
3.50	1.000	.167
6.00	1.000	.111
9.00	0.944	.111
11.50	0.833	.056
14.00	0.778	.056
15.50	0.722	.056
18.00	0.667	.056
22.00	0.611	.056
24.50	0.611	.000
30.00	0.556	.000
41.50	0.444	.000
70.00	0.389	.000
94.50	0.333	.000
116.00	0.278	.000
146.50	0.222	.000
159.00	0.167	.000
164.00	0.111	.000
285.00	0.056	.000
403.00	0.000	0.000

A total of 36 TRUS guided prostatic core biopsy specimen were studied. Out of 36 cases 18 cases were benign ie, Benign prostatic hyperplasia and 18 cases showed prostatic adenocarcinoma (Table-1). The percentage of positivity for adenocarcinoma is 50%.The mean age group for benign cases were 70.17(±7.79) and 68.22(±8.12) for malignant cases (Table-1). When considered the age of the patients in both group, there was no statistically significant variations among the groups (P>0.05), hence age was standardized in this research (Table-1). This study showed mean PSA value of 3.83(±5.43) in benign cases and 80.39(±99.07) in malignant cases and the result was statistically significant with p-value (<0.001) (Table-2). In addition, the mean serum PSA values were higher among malignant cases. In our study after analysis of gleason score and grade grouping it was found that out of 18 malignant cases one case were in gleason score 6 with grade group 1,5 cases were in score 7 with grade group 2,2 cases were in score 8 with grade group 4,9 cases were in score 9 with grade group 5 and single case had score of 10 with grade group 5 (Table-3). Mean PSA level was 108.80ng/ml in high risk group with gleason score of and more than 8. There was a statistically significant variation between low to intermediate risk group and high risk group on the basis of serum PSA levels (P<0.05)[Table 4]. The statistical significant value (P<0.01) clearly indicated that serum PSA levels significantly segregate the patients in terms of those who have malignant and those who have benign (Table 5). In our study the area under the curve is very close to 1 (AUC=0.972) (Figure-1). Therefore, the optimal cutoff value of serum PSA level was 9ng/ml in our study. We also found that Serum PSA level of 9 has the high sensitivity (0.944) and specificity of (0.889) (Table-6).

DISCUSSION

Our study showed that mean age of 68.22 ((±8.12) for prostatic adenocarcinoma which is consistent with studies done by Jemal A *et al*., and Khan MA *et al*., and there was no statistical significance [6, 7]. In our study the serum PSA levels were higher among cases diagnosed with prostatic adenocarcinoma and was statistically significant which is in concordant with studies done by Agarwal MS and Richie JP *et al*., [8, 9]. Our study showed that patients with high gleason score had significantly higher serum PSA levels. Studies done by Benson MC and Graham J also showed positive correlation between the PSA level and gleason scores [10, 11]. This proved that mean PSA levels play a significant role in diagnosing prostatic adenocarcinoma as well as in distinguishing benign from malignant cases. The optimum cut off adopted for serum PSA level is 4.0ng/ml for the screening purpose which is suggested by many studies [12, 13]. Using this cut off the sensitivity and specificity for detection of cancer cases were found to be 79% and 59% respectively [12, 13]. Han M *et al*., found positive predictive value of 32% with serum PSA level of 4 to 10ng/ml and 60% with serum PSA levels of more than 10ng/ml [14]. In our present study by Receiver operating characteristic curve analysis PSA cut off value to do biopsy was found to be 9ng/ml (Figure-1). It reveals that the diagnostic efficacy of serum PSA levels is high. It also showed a high sensitivity and specificity (Table-6) which is similar to observations done by Agnihotri S *et al*., and Yang WJ [15, 16].

CONCLUSION

Our study showed that for TRUS guided prostatic core biopsies serum PSA has significant role in segregating benign from malignant cases with an area under the ROC curve of 0.972.In our study the PSA cut point of 9 ng/ml showed high sensitivity and specificity.

REFERENCES

1. World Health Organization. Global Health Observatory. Geneva: World Health Organization; 2018. who.int/gho/database/ en/. Accessed June 21, 2018.
2. Ferlay J, Colombet M, Soerjomataram I, Siegel R, Torre L, Jemal A. Global and regional estimates of the incidence and mortality for 38 cancers: GLOBOCAN 2018. Lyon: International Agency for Research on Cancer. World Health Organization. 2018.
3. Carter HB, Pearson JD, Metter EJ, Brant LJ, Chan DW, Andres R, Fozard JL, Walsh PC. Longitudinal evaluation of prostate-specific antigen levels in men with and without prostate disease. Jama. 1992 Apr 22;267(16):2215-20.
4. Rocco B, Grasso A, Sosnowski R, dell'Orto PG, Albo G, Castle E, Coelho R, Patel V, Mottrie A. PSA mass screening: is there enough evidence?. Central European journal of urology. 2012;65(1):4-6.
5. Matlaga BR, Eskew LA, McCULLOUGH DL. Prostate biopsy: indications and technique. The Journal of urology. 2003 Jan 1;169(1):12-9.
6. Ahmedin Jemal DA, Tiwari RC, Murray T, Ghafoor A, Samuels A, Ward E, Feuer EJ, Thun MJ. Cancer statistics. 2004. CA Cancer J Clin. 2004;54(1):8-29.
7. Khan MA, Han M, Partin AW, Epstein JI, Walsh PC. Long-term cancer control of radical prostatectomy in men younger than 50 years of age: update 2003. Urology. 2003 Jul 1;62(1):86-91.
8. Agarwal MS, Sinha S, Juyal S, Gupta AK. Measurement of serum PSA in benign and malignant enlargements of prostate in Indian population: Relevance of PSAD in intermediate range PSA. Indian Journal of Urology. 2004 Jan 1;20(2):138-43.
9. Richie JP, Catalona WJ, Ahmann FR, M'Liss AH, Scardino PT, Flanigan RC, Dekernion JB, Ratliff TL, Kavoussi LR, Dalkin BL, Waters WB. Effect of patient age on early detection of prostate cancer with serum prostate-specific antigen and digital rectal examination. Urology. 1993 Oct 1;42(4):365-74.
10. Benson MC, Seong Whang I, Olsson CA, Mcmahon DJ, Cooner WH. The use of prostate specific antigen density to enhance the predictive value of intermediate levels of serum prostate specific antigen. The Journal of urology. 1992 Mar;147(3 Part 2):817-21.
11. Graham J, Baker M, Macbeth F, Titshall V. Diagnosis and treatment of prostate cancer: summary of NICE guidance. Bmj. 2008 Mar 13;336(7644):610-612.
12. Thickman D, Speers WC, Philpott PJ, Shapiro H. Effect of the number of core biopsies of the prostate on predicting Gleason score of prostate cancer. The Journal of urology. 1996 Jul;156(1):110-113.
13. Catalona WJ, Smith DS, Ratliff TL, Dodds KM, Coplen DE, Yuan JJ, Petros JA, Andriole GL. Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. New England Journal of Medicine. 1991 Apr 25;324(17):1156-61.
14. Han M, Partin AW, Pound CR, Epstein JI, Walsh PC. Long-term biochemical disease-free and cancer-specific survival following anatomic radical retropubic prostatectomy: the 15-year Johns Hopkins experience. Urologic Clinics of North America. 2001 Aug 1;28(3):555-65.
15. Agnihotri S, Mittal RD, Kapoor R, Mandhani A. Raising cut-off value of prostate specific antigen (PSA) for biopsy in symptomatic men in India to reduce unnecessary biopsy. The Indian journal of medical research. 2014 Jun;139(6):851-856.
16. Yang WJ, Lee DH, Chung BH, Cho JS, Choi YD, Kim SJ, Cho IR, Kim HS, Kim CI, Hong SJ, Severance Urologic Oncology Group. Detection rate of prostate cancer on biopsy according to serum prostate-specific antigen in Korean men: a multicenter study. Urology. 2006 Feb 1;67(2):333-6.