Usefulness of total prostate specific antigen, free/total prostate specific antigen ratio and high mobility group box protein 1 in prostate cancer patients

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Usefulness of total prostate specific antigen, free/total prostate specific antigen ratio and high mobility group box protein 1 in prostate cancer patients

Directed by Professor Oh Hun Kwon

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This master's thesis gave a thousand emotions crowded on my mind. Writing this thesis was like having lived a whole life with a fruitful life and desperate life sometimes.

Without regard to the result of this thesis, I learned a lot of things, especially prudence, through performing this experiment itself. And I realized that all the success was based on industry.

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ABSTRACT

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Prostate-specific antigen (PSA) assay has provided a simple means of monitoring the progress of prostate cancer (P.Ca), either before or after treatment. However, total PSA (t-PSA) lacks specificity for the P.Ca and does not correlate well between t-PSA and free/total PSA ratio (% f PSA). Because of the limitations of t-PSA and % f PSA for diagnosis of P.Ca, investigators have

searched for a new effective biomarker of P.Ca such as human glandular kallikrein (hK2), hK2/free PSA, free PSA/(t-PSA x hK2) ratios, complex PSA, prostate-specific acid phosphatase, P501S and ceruloplasmin.

The high mobility group box protein 1 (HMGB1) known as amphoterin is made up of chromatin-associated proteins and the concentration of HMGB1 in blood increased in many diseases including cancer, rheumatoid arthritis, and acute lung injury. Recent studies showed that mRNA expression of HMGB1 could be increased in P.Ca, especially in patients who have been treated with androgen deprivation hormone therapy. The aim of this study was to evaluate the clinical usefulness of serum t-PSA, % f PSA and HMGB1 levels using enzyme-linked immunosorbent assay (ELISA) in the diagnosis of P.Ca.

Twenty-nine of benign prostatic hyperplasia (BPH) patients (mean age, 71 yr; 60-84 yr), 34 of P.Ca patients (mean age, 70 yr; 55-86 yr) and 21 of normal healthy donors (mean age, 54.3 yr; 46-66 yr) were enrolled. Serum t-PSA and free PSA were measured by electrochemiluminescence immunoassay with E 170 module for Modular Analytics (Roche Diagnostics, Basel, Switzerland) and quantitative HMGB1 assay was measured by a 2-step sandwich (ELISA) with HMGB1 Kit (Shino-test, Kanagawa, Japan).

Serum t-PSA (P<0.0001) and % f PSA (P<0.0001), not HMGB1 (P=0.1938), were significantly different among P.Ca, BPH and healthy control groups without

regard to Gleason score and hormone treatment. HMGB1 (P=0.4701, 0.2415) was still not significantly different between P.Ca patient with or without hormone treatment. Serum HMGB1 of the P.Ca group with both low (≤7) and high (≥8) Gleason score did not show statistical difference with those of the BPH and healthy control group（P=0.2997; Gleason score≤7, P=0.1931; Gleason score≥8).

In conclusion, mRNA level of HMGB1 could be increased in P.Ca patients by androgen-deprived hormonal treatment or metastasis. However serum HMGB1 could not differentiate P.Ca patients with BPH and was not increased in P.Ca patients who had neither androgen deprivation hormonal treatment nor Gleason score≥8.

Key words: HMGB1, % f PSA, T-PSA, P.Ca, BPH

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I. INTRODUCTION

P.Ca is the 2nd leading cause of cancer death in the United States and has been recently increasing in Asia.[1,2] In 2006, the number of expected new cases was about 235,000 in the US. The need for the early detection of P.Ca has increased in both symptomatic and asymptomatic men all over the world. In the past decade, the widespread availability of serum PSA assay, digital rectal examination (DRE) and ultrasonography of prostate have provided a simple means of monitoring the progress of P.Ca. The American College of Physicians

guidelines suggest that patients should be referred to a urologist if an abnormality is noted on DRE or if serum PSA is more than 4 ng/mL for prostate biopsy.[3,4]

Since PSA lacks cancer specificity, elevated PSA concentrations are also observed in benign prostate diseases. This leads to a high number of false-positive findings in up to 60-80% of prostate biopsies and only 25–30% of men undergoing a biopsy are diagnosed with P.Ca in the 4–10 ng/mL PSA, “gray zone”. Moreover it was reported that serum PSA levels correlated with prostate volume and patients’ age in benign prostatic disease as well as P.Ca.[5, 6] Therefore, several strategies have been developed to improve the sensitivity and specificity of P.Ca diagnosis.

Using the % f PSA in t-PSA range of 4-10 ng/mL, approximately 20–25% of unnecessary biopsies can be avoided. However a recent meta-analysis critically reflected the use of %f PSA especially within the t-PSA gray zone, where only a very low %f PSA values truly indicate higher P.Ca risk.[7] Although some studies partially demonstrated correlations between % f PSA and stage or grade, an individual prediction of organ-confined (<T3a) or nonaggressive disease (Gleason score<7) is not possible to use % f PSA in other study.[8]

Because of the limitations of t-PSA and % f PSA in the diagnosis of P.Ca, investigators have searched for a new effective biomarker of P.Ca such as human glandular kallikrein (hK2), hK2/free PSA, free PSA/(t-PSA x hK2) ratios,

complex PSA, prostate-specific acid phosphatase, P501S and ceruloplasmin.[9-11] HMGB1 was first described in 1973 on the basis of electrophoretic separation properties of chromatin-associated proteins. It is a protein of approximately 30 kDa and is the major component of the non-histone nuclear protein group. It functions as a transcriptional regulator and is recently focused as a late inflammatory mediator. The major receptor of HMGB1 includes the receptor for advanced glycation end products (RAGE). The concentration of HMGB1 in blood is increased in many diseases including cancer, rheumatoid arthritis, acute lung injury, and disseminated intravascular coagulation.[12]

Some studies have investigated RAGE and HMGB1 RNA expression which was the ligand of RAGE, and advanced glycation end products (AGE)-RAGE function in P.Ca cells. It was also discovered that there were different expression patterns of RAGE and HMGB1 mRNA among untreated primary P.Ca tissue, BPH, and hormone-treated P.Ca.[13] Most studies on HMGB1 and P.Ca interaction have focused on RNA molecular levels with practical difficulty of clinical usefulness.

The aim of this study was to evaluate the clinical usefulness of serum t-PSA, % f PSA and HMGB1 levels using ELISA in the diagnosis of P.Ca patients.

II. MATERIALS AND METHODS

1. Patients and samples

Twenty-nine of BPH patients (mean age, 71 yr; range 60-84 yr), 34 P.Ca patients (mean age, 70 yr; range 55-86 yr) and 21 normal healthy donors (mean age, 54.3 yr; range 46-66 yr) were enrolled. Plasma specimens were collected from December 1, 2006 to October 24, 2007 at Yonsei University Severance Hospital.

Twenty-nine of BPH patients were classified into hormone-treated group (HTx, 15 patients) and untreated groups (No HTx, 14 patients). A total of 34 P.Ca patients were also classified into the HTx (16 patients) and No HTx groups (18 patients). Underlying diseases such as infectious disease, other inflammatory disease, and other combined neoplastic conditions were excluded.

Hormone treatment for P.Ca included gonadotropin releasing hormone (GnRH) agonist and oral anti-androgens allowing for the prompt blockade of androgen action on P.Ca during GnRH agonist use. In contrast with P.Ca, hormone treatment for BPH was 5alpha-reductase inhibitors suppressing dihydrotestosterone (DHT).

Table 1. Characterization of specimens enrolled

Group	Subgroup	Number of patients
BPH	HTx	15
	No HTx	14
P.Ca	HTx	16
	No HTx	18
Control		21
Total		**84**

2. Measurement of t-PSA, f- PSA and HMGB1

The t-PSA and f- PSA were measured by electrochemiluminescence immunoassay using the E 170 module for Modular Analytics (Roche Diagnostics, Basel, Switzerland) and Elecsys total and free PSA reagent kit (Roche Diagnostics, Indianapolis).

Quantitative HMGB1 assay employed a 2-step sandwich ELISA with HMGB1 Kit (Shino-test, Kanagawa, Japan). A polyclonal antibody specific for HMGB1 was briefly precoated onto the walls of the microtiter strips. A total of 100 μL of each standard dilution (pig HMGB1), positive control (pig HMGB1) and patient samples 100 μL were added to each wells. HMGB1 in samples binded specifically to the immobilized antibody. The plates were sealed with a thin

adhesive-coated plastic sheet and incubated for 20-24 hr at 37 °C. The unbound antibodies were removed by washing 5 times with PBS containing 0.05% Tween 20 (washing buffer). After washing, 100 μL/well of anti-human HMGB1 peroxidase-conjugated monoclonal antibody was added and the plate was incubated at room temperature for 2 hr. Then 2-color reagent (3,3′,5,5′-tetra-methylbenzidine and buffer containing additive 0.005mol/L hydrogen peroxide) of substrate solution were added to each well. The enzyme reaction proceed for 30 min at room temperature. The chromogenic substrate reaction was stopped by the addition of stop solution (0.35 mol/L sulfuric acid) and the absorbance was read at 450 nm within 60 min. The assay range for the HMGB1 ELISA was 2.5–80 ng/mL. The sensitivity of the ELISA method was 1 ng/mL and cross-reaction with HMGB2 was below 2% as specificity.

3. Statistical analysis

Data were expressed as median value and differences between groups were assessed for statistical significance using the Kruskal-Wallis statistic of non-parametric method. A *P*-value less than 0.05 denoted a statistically significant difference.

III. RESULTS

1. Comparisons of median values of t-PSA, % f PSA and HMGB1 among P.Ca group, BPH group and healthy control group

The median value of the t-PSA, % f PSA and HMGB1 of the BPH, P.Ca and healthy control groups are shown in Table 2. HMGB1 was not significantly different (*P*=0.1938) among the 3 groups compared but t-PSA and % f PSA were significantly different (*P*<0.0001).

Table 2. Comparisons of median values of serum t-PSA, % f PSA and HMGB1 among P.Ca group, BPH and healthy control groups

	Number of patients	t-PSA (ng/mL)	% f PSA	HMGB1 (ng/mL)
BPH	29	7.31	16.0	6.086
P.Ca	34	18.76	10.4	6.390
Healthy control	21	0.94	27.1	7.818
P-value		<0.0001*	<0.0001*	0.1938

*Significant difference (*P*<0.05).

T-PSA, total PSA; % f PSA, free PSA to t-PSA ratio; HMGB1, high mobility group box protein 1.

2. Comparisons of t-PSA, % f PSA and HMGB1 among hormone treated and untreated group of BPH and P.Ca

The median value of the t-PSA, % f PSA and HMGB1 of HTx-BPH, HTx-P.Ca and healthy control groups were evaluated and compared (Table 3). HMGB1 was not significantly different (P=0.2050) but t-PSA and % f PSA were significantly different (P<0.0001) among the 3 groups.

Table 3. Comparisons of median values of serum t-PSA, % f PSA and HMGB1 among HTx-BPH, HTx- P.Ca and healthy control groups

	Number of patients	t-PSA (ng/mL)	% f PSA	HMGB1 (ng/mL)
HTx-BPH	15	6.380	15.0	6.086
HTx-P.Ca	16	7.695	12.2	6.260
Healthy control	21	0.94	27.1	7.818
P-value		<0.0001*	<0.0001*	0.2050

*Significant difference (P<0.05).

T-PSA, total PSA; % f PSA, free PSA to t-PSA ratio; HMGB1, high mobility group box protein 1.

The median value of the t-PSA, % f PSA and HMGB1 for the No HTx-BPH, No HTx-P.Ca and healthy control groups were evaluated and also compared (Table 4). HMGB1 was not significantly different (P=0.2415) but t-PSA and % f PSA were significantly different (P<0.0001) among 3 groups.

Table 4. Comparisons of median values of serum t-PSA, % f PSA and HMGB1 among No HTx-BPH, No HTx-P.Ca and healthy control groups

	Number of patients	t-PSA (ng/mL)	% f PSA	HMGB1 (ng/mL)
No HTx-BPH	14	7.595	17.2	6.433
No HTx-P.Ca	18	29.465	9.2	6.649
Healthy control	21	0.94	27.1	7.818
P-value		<0.0001*	<0.0001*	0.2415

*Significant difference (P<0.05).

T-PSA, total PSA; % f PSA, free PSA to t-PSA ratio; HMGB1, high mobility group box protein 1.

3. Comparisons of median values of t-PSA, % f PSA and HMGB1 in Gleason score≤7 and Gleason score≥8 among No-Htx BPH, P.Ca and healthy control

groups

The No HTx-P.Ca group with Gleason score≤7, t-PSA (P=0.0622) and % f PSA (P=0.0507) did not show significant differences from the No HTx-BPH group but there were significant differences in the t-PSA (P<0.05) and % f PSA (P<0.05) between the No HTx-P.Ca (Gleason score≤7) and healthy control group (Table 5).

Table 5. Comparisons of median values of serum t-PSA, % f PSA and HMGB1 among No HTx-P.Ca, No HTx-BPH group and healthy control groups at Gleason score≤7

		t-PSA (ng/mL)		% f PSA		HMGB1(ng/mL)	
		Difference between median	2-tailed p	Difference between median	2-tailed p	Difference between median	2-tailed p
No HTx - BPH vs No HTx - P.Ca	14 vs 6	-7.90	0.0622	6.927	0.0507	0.519	0.7791
No HTx - P.Ca vs Healthy control	6 vs 21	15.682	0.0002	-17.158	0.0002	-1.688	0.4309
Healthy control vs No HTx - BPH	21 vs 14	-6.515	<0.0001	10.892	0.0047	1.905	0.1213

*Significant difference (P<0.05).

T-PSA, total PSA; % f PSA, free PSA to t-PSA ratio; HMGB1, high mobility group box protein 1.

In the No HTx-P.Ca with Gleason score≥8, t-PSA significantly increased by 63.28 ng/mL median difference (*P*=0.0013) and % f PSA significantly decreased by 9.692% median difference (*P*=0.0176) from the No HTx-BPH group. There were also significant differences of t-PSA increased by 74.992 ng/mL median difference (*P*=0.0018) and % f PSA decreased by 20.581 % median difference (*P*=0.0019) between the No HTx-P.Ca (Gleason score≥8) and healthy control group (Table 6).

Concerning the level of HMGB1, there were no statistical significance (*P*>0.05; from 0.1213 to 0.7791) in all of the comparisons.

Table 6. Comparisons of median values of serum t-PSA, % f PSA and HMGB1 among No HTx-P.Ca group, No HTX-BPH and healthy control group with Gleason score≥8

		t-PSA (ng/mL)		% f PSA		HMGB1(ng/mL)	
		Difference between median	2-tailed p	Difference between median	2-tailed p	Difference between median	2-tailed p
No HTx - BPH vs No HTx - P.Ca	14 vs 4	-63.280	0.0013	9.692	0.0176	-3.160	0.1575
No HTx - P.Ca vs control	4 vs 21	74.992	0.0018	-20.581	0.0019	1.472	0.7109
Healthy Control vs No HTx - BPH	21 vs 14	-6.515	<0.0001	10.892	0.0047	1.905	0.1213

*Significant difference (P<0.05).

T-PSA, total PSA; % f PSA, free PSA to t-PSA ratio; HMGB1, high mobility group box protein 1.

4. Comparisons of median values of t-PSA, % f PSA and HMGB1 among HTx and No HTx P.Ca groups

In Table 7, HMGB1 did not show the significant difference (P=0.4701) that had been discovered by another study as to mRNA HMGB1 expression in HTx P.Ca cells. However, t-PSA and % f PSA showed a significant difference (P<0.0001) among the 3 groups.

Table 7. Comparisons of median values of t-PSA, % f PSA and HMGB1 among HTx-P.Ca group, No HTx-P.Ca and healthy control groups

	Number of patients	t-PSA (ng/mL)	% f PSA	HMGB1 (ng/mL)
HTx – P.Ca	16	7.695	12.2	6.260
No HTx - P.Ca	18	29.465	9.2	6.649
Healthy Control	21	0.94	27.1	7.818
P-value		<0.0001	<0.0001	0.4701

*Significant difference (P<0.05).

T-PSA, total PSA; % f PSA, free PSA to t-PSA ratio; HMGB1, high mobility group box protein 1.

IV. DISCUSSION

Within the past few years, many studies have proven the additional value of the new biomarkers of P.Ca to enhance the discrimination between P.Ca and BPH.[14,15] A number of various biochemical marker have been studied for P.Ca, such as hK2, hK2/free PSA and free PSA/(t-PSA x hK2) ratios, complex PSA, prostate-specific acid phosphatase, P501S, and ceruloplasmin.[9-11]

HMGB1 has been studied as a cytokine mediator associated with inflammatory diseases but it has recently been evaluated as a new effective marker for various cancers. HMGB1 is the major component of the non-histone nuclear protein group and is known to be a transcriptional regulator. It acts on the specific receptor RAGE and induces prolonged inflammation, organ failure, septicemia and death.[16] Since its identification one-third of a century ago, the HMGB1 protein has been linked to various cellular processes, including release from necrotic cells and secretion by activated macrophages engulfing apoptotic cells. In the years since its discovery, HMGB1 has also been implicated in disease states, including Alzheimer's disease, sepsis, ischemia-reperfusion, arthritis, and cancer. In cancer, overexpression of HMGB1, particularly in conjunction with its receptor for advanced glycation end products, has been associated with the proliferation and metastasis of many tumor types, including breast, colon, melanoma.[17] Targeting the HMGB1 ligand or its receptor represents an important

potential application in cancer therapeutics, given its widespread overexpression, as well as that of its receptor in virtually every tumor type carefully examined.[18]

Initially it was hypothesized that increased RAGE-HMGB1 activity was elevated in all cancers, but recent studies have revealed that this increase is not always the case.[19] With confirmation of increased HMGB1 levels in most tumor cells, studies were done to determine whether it varied in tumor samples when compared with those found in normal cells.

In this study, serum HMGB1 (P=0.1938) did not show a significant difference but serum t-PSA (P<0.0001) and % f PSA (P<0.0001) did (Table 2). When a physician decides to proceed with HTx to high PSA patient with deferring the invasive biopsy procedure, HMGB1 could not avoid an invasive biopsy procedure nor provide a new possibility as a P.Ca marker.

Other studies reported that in cases of P.Ca, it does not increase HMGB1 levels and only androgen deprivation hormone therapy interact with HMGB1 and induce HMGB1 level rise only in P.Ca tissue but not in BPH, normal tissue. Primary cultured human prostatic stromal cells did not secrete HMGB1; however, HMGB1 secretion was induced by androgen deprivation by the luteinizing hormone–releasing hormone therapy, resulted in paracrine interaction between cancer and stromal cells through RAGE-HMGB1 interaction in patients with advanced P.Ca.[18] HMGB1-RAGE interactions have been examined in several

P.Ca cell lines, in hormone-refractory P.Ca tissues, and normal prostatic tissues. HMGB1 mRNA was expressed in all 3 cell lines from a hormone-independent P.Ca cell line expressing the highest level of RAGE mRNA. Untreated prostate carcinomas and hormone refractory prostate carcinomas in turn expressed higher RAGE and HMGB1 mRNA levels than normal prostatatic tissue.[13]

But in our study, Table 7 implicated that HMGB1 (P=0.4701) did not increase in the HTx P.Ca compared with the No HTx P.Ca group. Table 3 showed that HMGB1 (P=0.2050) had difficulty in differentiating P.Ca from BPH in patient followed up with HTx due to high serum PSA levels. Only t-PSA (P<0.0001) and % f PSA (P<0.0001) turned this impossibility into a possibility in this study and Table 4 showed that HMGB1 (P=0.2415) was unacceptable to screening biomarkers for P.Ca rather than t-PSA (P<0.0001) and %f PSA (P<0.0001) in No HTx groups.

In other investigations, expression of HMGB1 and RAGE in prostatectomy specimens from 40 patients with pT3 P.Ca including both metastasis and non-metastasis, preoperatively treated with luteinizing hormone–releasing hormone agonist, was increased in metastatic cases but not in non-metastatic cases. The majority of metastatic cases showed coexpression of RAGE and HMGB1 in tumor cells and stromal cells.[17, 20-22]

Table 6 showed that t-PSA (P=0.0013) and % f PSA (P=0.0176) could be used

to differentiate P.Ca from BPH in Gleason score≥8. And table 5 showed that t -PSA (P=0.0622) and % f PSA (P=0.0507) had a trend (almost P<0.05) to differentiate P.Ca from BPH in Gleason score≤7. When compared with the control group, t-PSA (P<0.05) and % f PSA (P<0.05) can be used in all P.Ca patients without regard to Gleason score. But HMGB1(P>0.05) could not used to differentiate P.Ca from BPH both in Gleason score≤7 and Gleason score≥8.

Serum total PSA has been the most useful predictor of P.Ca[23] and % f PSA could enhance the specificity of differentiating P.Ca from BPH, through a lot of studies based on a significant number of men.[24-26] However, the total P.Ca and BPH patients in this study was 63 patients and this patient number may be too insufficient to demonstrate the significant difference statistically. The lack of patient number in this study may cause the table 5 result, slightly above or below the level of P<0.05. In this reason, this study need to be replenish with more patients to show the significant difference of t-PSA, % f PSA and HMGB1 in differentiation of P.Ca patients from BPH patients without regard to Gleason score.

V. CONCLUSION

Although mRNA level of HMGB1 could be increased in P.Ca treated with androgen-deprived hormonal treatment or metastasis, serum HMGB1 could not increased in P.Ca patients who had neither androgen deprivation hormonal treatment nor Gleason score≥8. And serum HMGB1 couldn’t differentiate P.Ca patients with BPH.

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ABSTRACT (IN KOREAN)

전립선 암 환자의 total Prostate Specific Antigen, free/total PSA ratio 및 High mobility group box protein 1의 진단적 유용성 평가

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이성실

Prostate Specific Antigen(PSA)은 전립선 암의 치료전이나 치료후의 암 진행의 추적의 간단한 방법으로 사용되어왔다. 그러나, 총 PSA (total PSA, t-PSA)는 전립선 암에 대한 특이도가 부족하고 총 PSA와 % 자유성 PSA (free/total PSA, % f PSA)의 상관성이 부족하다. 전립선 암의 진단에 있어서, 총 PSA와 % 자유성 PSA의 제한점 때문에 여러 연구자들이 전립선 암의 진단을 위하여 human glandular kallikrein (hK2), hK2/free PSA and free PSA/(t-PSA x hK2) ratios, complex PSA, prostate-specific acid phosphatase, P501S, ceruloplasmin 등의 새로운 효과적인 표지자 연구를 시도해왔다.

High mobility group box protein 1 (HMGB1) 단백은, 과거 ampoterin으로 알려져 있었고, chromatin-관련 단백이다. 혈중 HMGB1 농도는 악성종양, 류마토이드 관절염, 급성 폐 손상에서 증가한다. 최근 여러 연구에서 HMGB1의 mRNA 발현이 안드로젠 박탈 호르몬 처리된 전립선 암 세포에서 증가하는 사실이 밝혀졌다.

이 연구의 목적은 혈장 총 PSA, % f PSA와 ELISA(enzyme-linked immunosorbent assay) 법을 이용한 혈장 HMGB1 농도의 임상적 유용성을 평가하는 것이다.

전립선 암의 생지표의 개발의 필요성과 더불어, 이 연구에서는, 전립선 조직검사로 확진 받은 전립선 암 환자에서 혈장 HMGB1 농도가 측정되었다. 대상은 29명의 전립선비대증환자 (평균나이 71세, 60-84세), 34명의 전립선 암 환자 (평균나이 70세, 55-86세), 21명의 정상군 (평균나이 54.3세, 46-66세)이었다.

총 PSA와 자유성 PSA는 화학발광 면역분석법으로 측정되었다. 이는 E 170 module for Modular Analytics (Roche Diagnostics, Basel, Switzerland)를 이용하였다. 정량적 HMGB1 분석은 두 단계 ELISA법을 이용한 HMGB1 Kit(Shino-test, Kanagawa, Japan)를 이용하였다.

Gleason score와 호르몬 치료 여부와 무관하게 전립선 암, 전립선비대증과 정상군 사이에서 혈장 HMGB1 (P=0.1938)이 아닌, 총 PSA (P<0.0001)과 % 자유성 PSA (P<0.0001)는 유의한 차이를 보였다.

HMGB1 (P=0.4701)은 호르몬 치료를 받은 전립선 암 군과 호르몬 치료를 받지 않은 전립선 암 군에서 여전히 유의한 차이를 보이지 않았다. 또한 전립선비대증과 정상군과 비교하였을 때, 전립선 암은 Gleason score이 낮은 군(≤7)과 높은 군(≥8)에서 모두 HMGB1은 통계학적으로 유의한 차이를 보이지 않았다 (P=0.2997, P=0.1931).

결론적으로, 환자의 혈장을 사용하는 HMGB1 ELISA kit는 의료인들에게 검사이용의 편의성을 제공하지만 HMGB1은 진단에 있어서 총 PSA 와 % 자유성 PSA보다 우월하지 않다. 왜냐하면, 전립선 암 환자군을 전립선비대증과 정상군과 비교하였을 때, HMGB1은 통계학적으로 총 PSA 와 % 자유성 PSA보다 더 유의한 차이를 보이지 않았기 때문이다.

핵심되는 말: HMGB1, % f PSA, t PSA, 전립선 암, 전립선비대증