FREE PROSTATE SPECIFIC ANTIGEN (fPSA) AND THE VALUE OF FREE/TOTAL PSA RATIO IN BENIGN NODULAR PROSTATIC HYPERPLASIA AND PROSTATIC CARCINOMA

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Abstract

Background: Besides tPSA, the f/t PSA ratio plays a meaningful role for the orientation of diagnosis and the screening of the prostatic diseases, especially for the 2 most frequent ones including prostatic carcinoma and benign nodular hyperplasia. **Objectives**: - To compare the average mean of the f/t PSA in the patient with the prostatic carcinoma and benign nodular hyperplasia; - To determine the diagnostic value of the f/t PSA in prostatic carcinoma. **Materials and Method**: Cross-sectional study on 70 patients including 35 cases with benign nodular prostatic hyperplasia and 35 ones with carcinoma of the prostate. **Results**: The average mean of the fPSA in the patient with the prostatic carcinoma was higher than ones with the benign nodular hyperplasia (7.06ng/ml, 1.08ng/ml respectively); The f/t PSA ratio of prostatic carcinoma (0.15) was lower than ones of benign nodular hyperplasia (0.25); in most patients with benign nodular hyperplasia the f/t PSA ratio was over 0.19 (88%), otherwise in the PC group it was below 0.19 (71.11%). With the cut-off value of 0.19 of the f/t PSA ratio, the sensitivity, specificity, accuracy were 91.43%, 62.85% and 77.14% respectively. **Conclusions**: f/t PSA Ratio should be applied for the diagnosis and the screening of the prostatic tumors apart from the tPSA test.

Key words: *Prostate Gland, PSA (Prostate Specific Antigen), tPSA (total PSA), fPSA (free PSA), f/t PSA Ratio, prostatic carcinoma (PC), benign nodular prostatic hyperplasia.*

1. INTRODUCTION

Prostatic carcinoma was one of the most common type of male cancer in the world, accounting for 15% of the new cases and the second rage after lung cancer with 1.1 millions patients now and 307.000 of deaths [8]. In Vietnam, although PC was not the frequent one, this cancer was not rare and ever increasing, especially for the men after 50 years old [8], [20]. Among many methods to early discover this disease with no or minimum intervention such as clinical examination, ultrasound, cytopathology or biopsy, the serum tPSA test was applied in routine for the diagnosis and the screening of the prostatic tumors [3], [6], [9], [10], [12], [13], [20]. Recently, in order to increase the ability of the diagnosis and the screening there were the researches of the new index of PSA, among these the f/t PSA ratio plays a meaningful role to enhance the specificity of tPSA especially with the level of 4-10ng/ml as well as to reduce unnecessary biopsies in patients undergoing evaluation for prostate cancer [2], [4], [5]. In Vietnam there were some reports of this disease, but the study of f/t PSA ratio was limited [10], [11], [12], [15]. With the important role of the f/t PSA ratio in the prostatic cancer diagnosis, we carried out this study aiming to:

- To compare the average mean of the f/t PSA in the patients with the prostatic carcinoma and benign nodular hyperplasia;

- To determine the diagnostic value of the f/t PSA in prostatic carcinoma.

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2. MATERIALS AND METHOD

Cross-sectional study on 70 patients including 35 cases with benign nodular prostatic hyperplasia and 35 ones with carcinoma of the prostate diagnosed definitely by histopathology at Hue Central Hospital and the Hospital of Hue University of Medicine and Pharmacy.

The fPSA and tPSA were carried out before the operation and the other interventions.

The excluding cases: prostatic inflammation, injury or the patients with the history of benign nodular prostatic hyperplasia or prostatic carcinoma treated by cystostomy, chemotherapy, pelvic radiation, prostatic operation.

2.1. Histopathology

The operation pieces were treated by the standard histopathological technique which fixed in 10% neutral formalin, embedded in paraffin, cut in 3µm thickness and stained by H.E.

The slides were interpreted under the microscopy by 2 experience pathologists independently.

Benign nodular prostatic hyperplasia classified by WHO 2004 [11] and prostatic cancer by modified Gleason 2005 [7].

2.2. PSA measuring

fPSA and tPSA were measured with the Elisa sandwich immunologic reaction principle by the Cobas 6000 machine, the substance used by Roche company [17], [18].

The f/tPSA ratio divided into 2 groups following [15], [20]:

- Group 1: The f/tPSA ratio ≤ 0.19 (suspected malignant)
- Group 2: The f/tPSA ratio > 0.19 (oriented to benign)

Calculating the sensitivity, specificity, accuracy of the f/t PSA ratio.

3. RESULTS

3.1. Comparing the average mean of the f/t PSA ratio in the patients with the prostatic carcinoma and benign nodular hyperplasia

Table 3.1. Average mean concentration of tPSA and fPSA

Disease	tPSA (ng/ml)	fPSA (ng/ml)
Prostate carcinoma	71.85	7.06
Benign nodular hyperplasia	5.01	1.08
p	p < 0.05	p < 0.05

Prostate carcinoma: the highest level of tPSA was 193.41ng/ml, the lowest 2.25, average 71.85ng/ml

Benign nodular hyperplasia: the highest level of tPSA was 27.68ng/ml, the lowest 0.395, average 5.01ng/ml.

Table 3.2. f/t PSA ratio

Disease	tPSA ng/ml	fPSA ng/ml	f/t PSA ratio
Prostate carcinoma	71.85	7.06	0.15
Benign nodular hyperplasia	5.01	1.08	0.25
p			p < 0.05

Prostate carcinoma: the highest, lowest and the average f/tPSA ratio were 0.75; 0.01, and 0.15 respectively.

Benign nodular hyperplasia: the highest, lowest and the average f/tPSA ratio were 0.58, 0.03 and 0.25 respectively.

Table 3.3. Comparing the average mean of the f/t PSA in the patients with the prostatic carcinoma and benign nodular hyperplasia

f/tPSA	benign nodular hyperplasia		prostatic carcinoma		p < 0.01
	n	(%)	n	(%)	
≤ 0.19	13	28.89 %	32	71.11 %	
>0.19	22	88 %	3	12%	

The table showed that most patients with benign nodular hyperplasia the f/t PSA ratio were over 0.19 (88%). Otherwise in the PC group they were below 0.19 (71.11%).

3.2. Diagnostic value of the f/t PSA in prostatic carcinoma

Table 3.4. Diagnostic value of the f/t PSA in prostatic carcinoma (with the cut-off ≤ 0.19)

Results	n
True positive	32
False positive	13
True negative	22
False negative	3
Total	70

With the cut-off of 0.19 of the f/t PSA ratio, the sensitivity, specificity, accuracy were 91.43%, 62.85% and 77.14% respectively.

4. DISCUSION

4.1. Comparing the average mean of the f/t PSA ratio in the patients with the prostatic carcinoma and benign nodular hyperplasia

Comparing to the benign nodular hyperplasia, in the patients with prostate carcinoma, the tPSA concentration was higher and the fPSA was lower so the f/tPSA ratio was lower in cancer group. The most acceptable theory was that in the cancer patients, PSA penetrated into the blood vessel by many more ways than in the benign ones [12], [19]. In the benign nodular hyperplasia, before reaching the blood vessel, PSA had stayed in the intercellular space so that it was decomposed by the proteolytic cleavage enzymes [1]. Otherwise in the cancer tissue, the PSA going to the blood stream by the activated one combining with the anti-protease agents so it was not deteriorated and thus tPSA was always in higher level [12], [19].

Our research showed that the fPSA in the cancer group was 7.06ng/ml, higher than that in benign one (1.08ng/ml). The differentiation was significant ($p < 0.05$). For average mean of the f/t PSA ratio the cancer was lower than the benign one (0.15 and 0.25 respectively, $p < 0.05$), in most patients with benign nodular hyperplasia the f/t PSA ratio was over 0.19 (88%), otherwise in the PC group it was below 0.19 (71.11%).

The serum tPSA test was applied in routine for the diagnosis, the screening and the treatment assessment of the prostatic carcinoma. Because the tPSA was also increasing in the patients without prostatic cancer such as benign tumours or inflammation, the malignant diagnosis was not accurate in the case of light increasing level of tPSA .

Recently, in order to increase the ability of the diagnosis and the screening, especially in these cases of tPSA level of 4-10ng/ml, the f/t PSA ratio was applied [4], [16].

According to Catalona, if the fPSA decreased compared to the tPSA, the malignant risk was increasing. Using the fPSA increased the sensitivity of the PSA with the normal level and the specificity with the level of 4-10 ng/ml [5].

In Vietnam, according to Dao Thi Hong Nga et al, the average mean of f/tPSA ratio in the healthy male was 0.27 ± 0.08 and in all the PC patient it was < 0.19 [15].

Naz S et al report showed that 80% of PC patients the cut-off of the f/tPSA ratio were below 0.18 and it was over 0.18 for 75% of benign nodular hyperplasia [14].

Catalona, with the f/tPSA ratio < 25% it could discover 95% of PC cases [5].

All indicated that the fPSA and the f/tPSA ratio were meaningful in order to discover and differentiate between the PC patients and the benign nodular hyperplasia ones.

4.2. Diagnostic value of the f/t PSA in prostatic carcinoma

In our study with the cut-off value of 0.19 of the f/t PSA ratio, the sensitivity, specificity, accuracy were 91.43 %, 62.85 % and 77.14 % respectively.

In the world, the threshold of f/t PSA ratio was changeable but in general it was from 0.15 to 0.20 [4]. According to Barut et al, with the cut-off value of 0.17 the sensitivity 90% and the specificity 78% [2]. In the Thakur V et al report, with the cut-off of 0.16 the sensitivity 85% and the specificity 67% [19].

In Vietnam, compared to the other authors like Dao Thi Hong Nga, Nguyen Van Hung our results were the same [10], [15].

In addition to the tPSA test, the fPSA and the

f/tPSA ratio showed that the sensitivity was very high (over 90%) and the specificity was also high (over 62%), therefore they should be put into practice in the suspected cases of prostate cancer.

5. CONCLUSION

Researching on 35 cases of PC and 35 ones of benign nodular hyperplasia, it showed that:

The average mean of the fPSA in the patients with the prostatic carcinoma was higher than ones with the benign nodular hyperplasia (7.06ng/ml, 1.08ng/ml respectively); The f/t PSA ratio of prostatic carcinoma (0.15) was lower than ones of benign nodular hyperplasia (0.25); in most patients with benign nodular hyperplasia the f/t PSA ratio was over 0.19 (88%), otherwise in the PC group it was below 0.19 (71.11%).

With the cut-off of 0.19 of the f/t PSA ratio, the sensitivity, specificity, accuracy were 91.43 %, 62.85% and 77.14% respectively.

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