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Original Research

Interest of Digital Rectal Examination and PSA Assay in the Early Detection of Prostate Cancer at the University Teaching Hospital of Brazzaville

Intérêt du Toucher Rectal et du Dosage de PSA dans la Détection Précoce du Cancer de la Prostate au Centre Hospitalier et Universitaire de Brazzaville

Loungouala Sounda Bernaud Sedwige[1,2], Ngombe Mouabata Dorine Florence Luthera[3], Loubano Voumbi Ghislain[4], Odzebe Anani Wencesl Severin[1,5], Biyama Kimia Paule Flora[2], Moukassa Donatien[1,6], Gauchez Anne-Sophie[7]

1 : Faculty of Health Sciences, University Marien Ngouabi, Brazzaville, Republic of Congo
2 : National Public Health Laboratory, Brazzaville, Congo
3 : Faculty of Sciences and Techniques Mohammedia, University Hassan II of Casablanca, Casablanca, Morocco
4 : Medical Analysis Laboratory, Dolisie General Hospital, Dolisie, Congo
5 : Department of Urology, University Hospital Center of Brazzaville, Congo
6 : General Edith Lucie Bongo Hospital, Oyo, Congo
7 : Grenoble-Alpes Hospital, Pole of Biology, 38043 Grenoble cedex 9

Corresponding author
Loungouala Sounda Bernaud Sedwige, Email: loungsedwige@gmail.com, Tel:+242066284266

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Mots clés : Toucher Rectal, PSA, Cancer de la Prostate, diagnostic précoce.

ABSTRACT

Objective. To assess the effectiveness of Digital Rectal Examination and the PSA testing in the early detection of prostate cancer. **Patients and methods.** Prospective, analytical and descriptive study conducted at the University Hospital Center of Brazzaville in the urology department and in the urology-andrology outpatient clinic during the period from December 1st, 2016 to May 31st, 2017. Of the 210 patients who came for consultation, 77 patients were selected, representing 36.7%. Clinical, biological, ultrasound aspects were the variables of the study. **Results.** The mean age (SD) of the patients was 67.83 years (52-84 years). The 70-79 age group was the most represented at 40,20%. The Digital Rectal Examination (DRE) was abnormal in 74% of the cases, the average level of PSA was 77.12 ± 125.79 ng/ml; 55.84% of patients had a PSA level higher than 10 ng/ml. The detection of prostate cancer is 16.9% in patients with normal PSA and normal DRE and 9.1% with high PSA, it is 10.4% with normal PSA and abnormal DRE and 62.9% with high PSA and abnormal DRE. The Gleason score was greater than 7 in patients with PSA<4 ng/ml, between 4-10 ng/ml and >10 ng/ml in 2.6%, 3.9% and 40.3% respectively. A good agreement was observed between PSA level and DRE (p=0.00008). **Conclusion.** The combination of DRE and PSA improves the early detection rate of prostate cancer.

RÉSUMÉ

Objectif. Évaluer l'efficacité du toucher rectal et du dosage de PSA dans la détection précoce du cancer de la prostate. **Patients et méthodes.** Étude prospective, analytique et descriptive, réalisée au Centre Hospitalier et Universitaire de Brazzaville dans le service d'urologie et en consultation externe d'urologie-andrologie durant la période du 1er décembre 2016 au 31 mai 2017. Sur les 210 patients venus en consultation, 77 patients ont été sélectionnés. Les aspects cliniques, biologiques, échographiques ont été les variables de l'étude. **Résultats.** L'âge moyen des patients est de 67,83 ans. La tranche d'âge 70-79 ans était la plus représentée (40,2%). Le toucher rectal (TR) est anormal dans 74% des cas, le taux moyen de PSA était de 77,12 ± 125,79 ng/ml; 55,84% des patients ont un taux de PSA supérieur à 10 ng/ml. La détection du cancer de la prostate est de 16,9% chez les patients avec un taux de PSA normal et un TR normal et de 9,1% avec un taux de PSA élevé, il est de 10,4% avec un taux de PSA normal et un TR anormal et de 62,9% avec un taux de PSA élevé et un TR anormal. Le score de Gleason est supérieur à 7 chez les patients avec un taux de PSA< 4 ng/ml, 4-10 ng/ml et >10 ng/ml respectivement dans 2,6%, 3,9% et 40,3%. Une bonne concordance a été observée entre le taux de PSA couplé au TR (p=0.00008). **Conclusion.** La combinaison TR-PSA améliore le taux de détection précoce du cancer de la prostate.

INTRODUCTION

Prostate cancer (PCa) is a disease of the elderly and a major public health problem in developed countries **[1]**. Worldwide it is the second most frequently diagnosed cancer in men and the fifth leading cause of cancer death **[2, 3, 4]**. In the Republic of Congo, according to the 2013's cancer registry, prostate cancer is the second most common cancer in men **[5, 6]**.

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HIGHLIGHTS

What is already known on this topic

Numerous studies based on the practice of digital rectal examination (DRE) and serum prostate specific antigen (PSA) have led to the combination of these two diagnostic tools to increase their sensitivity and specificity in the detection of prostate cancer, allowing diagnosis of the disease at a localized stage, curable by surgical or radio-therapeutic treatment

What question this study addressed

Value of DRE and the PSA testing in the early detection of prostate cancer in Congo.

What this study adds to our knowledge

Prostate cancer detection was 62.9% with an elevated PSA level and an abnormal digital rectal examination. The combination of DRE and PSA improved diagnosis.

How this is relevant to practice, policy or further research.

Comparative study between PSA, free PSA, free PSA/total PSA ratio, 2proPSA, TR: diagnostic values may be useful.

The first line of screening is represented by the Digital Rectal Examination (DRE) and the prostate specific antigen (PSA) assay **[7]**. Prior to PSA, the only tool for early detection of PCa was the DRE, which is described as simple to perform and non-invasive, relatively inexpensive, many men destined to die of PCa did not have palpable abnormalities **[8]**. DRE does not allow manual palpation of the entire prostate and therefore detects disease when it is no longer confined to the organ. After the introduction of PSA as an early detection test, it is now a well-established tumor marker that contributes to the early diagnosis, implementation and follow-up of PCa superior to prostatic acid phosphatase despite its low specificity related to various factors influencing its interpretation **[9]**. In clinical practice, biopsies are usually performed only when the results of a PSA and/or DRE are abnormal, which leads to a misdiagnosis in most small PCa. PCa is often asymptomatic in the localized stage and may be revealed by the following clinical signs: urinary frequency, urinary retention, hematuria, dysuria, or sometimes by bone pain or other organ dysfunction or failure indicating a secondary location. Numerous international studies based on the practice of DRE and serum PSA have led to the combination of these two diagnostic tools to increase their sensitivity and specificity in the detection of prostate cancer **[9, 10]**. These two tools constitute an evolution, allowing diagnosis of the disease at a localized stage, curable by surgical or radio-therapeutic treatment **[11]**.

In Congo, unfortunately, diagnosis is late and at an advanced stage of the disease. It is through the latter that we undertook the current study to evaluate the effectiveness of DRE and PSA testing, two tools that are readily available in our country, in the early detection of prostate cancer.

PATIENTS AND METHODS

Patients

It was a prospective, analytical and descriptive study conducted over a period of six (06) months, that is from December 1st, 2016 to May 31st, 2017 in the urology department of the University Teaching Hospital of Brazzaville (CHU-B) and in the urology - andrology outpatient clinic. Patients being 50 years old or older, coming to the outpatient clinic for suspected prostate cancer, consenting in writing and whose medical record including clinical, biological, radiological and histological elements were included.

All non-consenting patients or patients with incomplete records were not included.

This study was approved by the ethics committee of the National Institute for Research in Health Sciences (IRSSA) of Brazzaville.

Methods

The clinical investigation consisted of an interrogation (age, family history of PCa) and a clinical examination (reason for consultation, digital rectal examination). The para-clinical survey consisted in the exploitation of the results of biological (total PSA, prostate biopsy) and morphological (ultrasound) examinations contained in the medical files.

The variables studied were: reason for consultation, prostate characteristics on digital rectal examination, total PSA level, histological type, gleason score, capsular invasion of PCa, type of ultrasound, ultrasound characteristics of the prostate, prostate weight.

The interpretation of the kappa test concordance coefficient depended on the calculated value of the K coefficient: Discordance between two tests (DT), $k \leq 0$; Very poor concordance (TFC), $0<k\leq0.2$; Poor concordance (FC), $0.2<k\leq0.4$; Moderate concordance (CM), $0.4<k\leq0.6$; Good concordance (BC), $0.6<k\leq0.8$; Excellent concordance (EC), $0.8<k\leq1$

Microsoft Excel within its 2013 version, Graph Pad Prism version 5.0.0.3, and SPSS version 20 were used. Results are expressed as mean ± SD for quantitative variables and as headcount and/or percentage for qualitative variables. The comparison of qualitative variables was done by the Pearson and Fischer test (chi2). The comparison of quantitative variables was done by the student test (t-test). The p-value was calculated with the data comparison program that uses the chi2 and t-test. The p-value was used to assert that there was a significant difference between two numbers or two means. In this case, its value was less than or equal to 0.05. A confidence interval of 95% was used to calculate the results.

RESULTS

During the study period, two hundred and ten (210) randomly selected patients were consulted. After interview and review of medical records, seventy-seven (77) patients with histological prostate cancer were selected, representing a frequency of 36.6%. The mean (SD) of age was 67.83 ± 7.83 years (range 52 - 84 years). The median age was 69 years. The range age of 60 to 69 years (36.4%) and 70 to 79 years (40.20%) were predominant (**figure 1**).

23.4% of patients have a family history of PCa (13% are farmers). 54.5% of the patients came to the clinic mainly for dysuria, only 2.6% for voluntary screening for PCa. The characteristics of the DRE showed 90.9% of DRE

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with a benign appearance and 9.1% with a malignant appearance. The DRE was normal in 26% of cases and abnormal in 74%. The prostate capsule was invaded in 76.6% of cases. For a PSA concentration between 4-10ng/ml or >10 ng/ml respectively 1.3% and 22.1% of the patients had capsular invasion (p=0.17233).

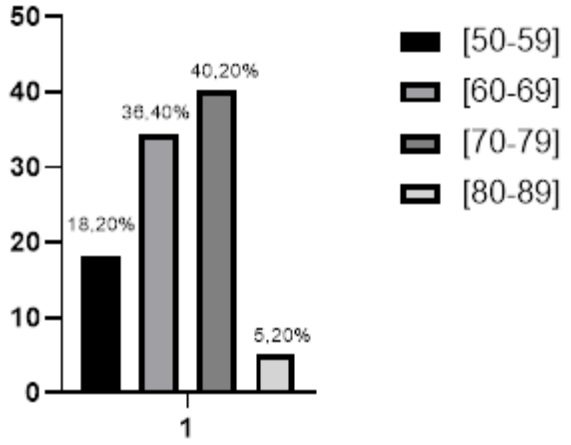

Figure 1: Distribution of patients by age group.

The mean PSA level was 77.12 ± 125.79 ng/ml (3 - 911 ng/ml), the median is 40 ng/ml. PCa was detected in 27.3%, 16.9%, 55.8% of the cases in patients with PSA < 4ng/ml, 4-10 ng/ml; and > 10ng/ml respectively.

The majority of PCa patients were in the age range of 60-69 years and 70-79 years respectively for PSA < 4ng/ml (15.6%) and 4-10 ng/ml (7.8%), > 10ng/ml (29.9%) (p=0.00704). The PCa detection rate was 16.9% in patients with normal PSA and normal DRE and 9.1% with high PSA, it was 10.4% with normal PSA and abnormal DRE and 62.9% with high PSA and abnormal DRE (p=0.0008).

Histological analysis concluded prostatic adenocarcinoma in 100% of cases. The mean (SD) Gleason score (GS) was 7.22 ± 1.69 with a median of 7 and extremes of 3 and 10. 46.8% of patients had poorly differentiated CaP. The Gleason score was greater than 7 in patients with PSA < 4ng/ml, 4-10 ng/ml, > 10ng/ml in 2.6%, 3.9% and 40.3% respectively (p=0.10210).

56 patients out of 77 underwent ultrasound: 60.7% endorectal ultrasound and 39.3% transpubic ultrasound. The structure was homogeneous and the contour regular in 69.6% and 66.1% respectively. The mean (SD) weight of the prostate was 44.85 ± 36.35g with a median weight of 34.5g. This ranged from 15 to 193g. For normal and benign DRE (Benign Prostatic Hypertrophy) the echostructures were homogeneous respectively in 17.9% and 50% and for malignant DRE 10.7% of echostructures were heterogeneous (p=0.00167). For a PSA level < 4 ng/ml, 4-10 ng/ml of echostructures are homogeneous respectively 17.9% and 14.3%; in contrast to a PSA level > 10 ng/ml, 25% of echostructures are heterogeneous (p=0.11081).

DISCUSSION

In our study, the relative frequency of PCa was 36.6%; the mean age of diagnosis of PCa was 67 ± 7.83 years. The distribution by age range indicated a high frequency of this cancer in the 60 to 69 (36.4%) and 70 to 79 (40.2%) age groups. Other studies led to prostate cancer, basically those of Tze Kiat Ng et al **[12],** Levent Verim et al **[13]** and Deep Par Kash et al **[14]** reported a relative frequency of 52%, 53.6% and 50.3% respectively. These differences could be explained by the fact that these studies were conducted over long periods of time, thus increasing their relative frequencies. Konan et al **[15]**, Peko et al **[16]** reported a frequency similar to ours in 31.3% and 36.24% respectively. Khalid Al et al **[10]** and Selsuk Sarikaya et al **[17]** reported a frequency of 27.8% and 17.8% respectively. The high frequency of our study compared to the others is indicative of the current situation of the disease in Congo or at least in Brazzaville. Niang Sylla et al **[18],** Khalid et al **[10]** found lower mean ages of 65.5 and 64.1 ± 7.4 years respectively. Berroukche et al **[19]** who reported 35.8% in the 60-69 age group. Our results are similar to those of Ojewola RW et al **[20]** who reported an average age of 67.9 years.

The unswerving aspect of the prostate was noted in 90.9% of cases. This aspect did not correlate significantly with the Gleason score and capsular breakthrough. Claartje Gosselaar et al **[8]** reported in three experience series patients with PCa with a benign looking DRE in 71%, 92% and 93% of cases respectively.

A review of the literature on PCa has shown that when DRE alone is used, more than 50% of the tumors detected are locally advanced on pathological examination. Deep Par Kash et al **[14]** reported an observation that abnormal DRE was associated with a higher chance of finding an aggressive PCa. Furthermore, 23-45% of cancers would be missed if the indication for biopsy was based on DRE alone. The DRE alone is therefore an insufficient tool for screening but it remains a requisite tool for the diagnosis of prostate cancer. Indeed, 25% of cancers can be detected by DRE when the PSA is normal. The accuracy of DRE in the diagnosis of PCa has been documented as 39-45% in clinical studies **[20].**

In contrast to our PSA results, a Spanish study reported a PCa detection of 48.61%, 25.11%, 21.4% for patients with PSA levels >10 ng/ml, 4-10 ng/ml, and <4 ng/ml respectively **[21].** Deep Par Kash et al **[14]** reported a mean PSA level of 23.8 ± 10.5 ng/ml in patients with PCa with PSA levels <4 ng/ml, 4-10 ng/ml, 10.01-20 ng/ml, >20 ng/ml in 56.5%, 19.1%, 28.3% and 74,6% respectively**.** It is observed that the detection rate of PCa increased with the level of PSA. Some studies have reported the hypothesis that the probability of the presence of PCa is almost low at a normal PSA value. The existence of cancer at a normal PSA level of 4 ng/mL could be explained by the loss of the ability of anaplastic cells to secrete PSA.

In our study, we found a statistically significant difference between serum PSA and DRE (p=0.0008). Our results corroborate with those of Selsuk Sarikaya et al **[17]** who reported lower values in patients with normal PSA and abnormal DRE and high PSA with abnormal DRE in 8.7%

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and 49.3% respectively. Deep Par Kash et al **[14]** reported the results similar to ours in patients with high PSA and abnormal DRE in 61.2%.

Tze Kiat Ng et al **[12]** reported a detection rate of PCa in patients with normal DRE and PSA in PSA levels <4 ng/ml, 4-10 ng/ml, >10 ng/ml was 9%, 31% and 48% of cases respectively; this detection rate in patients with the proportion of patients with abnormal DRE and the same PSA levels was 27%, 67% and 85%, respectively. Results from numerous studies have stated that the raise in serum PSA level increases with the incidence of prostate cancer and have highlighted the important role of DRE combined with PSA in improving the diagnosis of PCa. The most common indications for positive biopsies were a combination of an elevated PSA level and an abnormal DRE **[20].**

Selsuk Sarikaya et al **[17]** reported a Gleason score greater than 7 in 33%, 13.8%, 46.7% of patients with PSA levels <4 ng/ml, 4-10 ng/ml, >10 ng/ml respectively. There was a positive correlation between the different levels of PSA and the tumor stage; the higher the PSA level, the less differentiated the cancer. Regarding the Coefficient of concordance kappa k, the current study found that high PSA levels, abnormalities of DRE (k=0.099) and prostatic ultrasound (k=0.22) are associated with suspected prostatic tumor.

CONCLUSION

Prostate cancer is a pathology of insidious evolution. Any clinical expression can be in favor of a locally advanced or metastatic stage. The majority of patients in Republic of Congo consult at a late stage and the voluntary screening rate was 2.6%. 90.9% of all DRE performed in patients with PCa are benign and 55.8% of patients have a PSA level above 10 ng/ml. An elevated PSA level and an abnormal DRE is present in 62.9% of patients. The characteristics of the DRE and the level of the different PSA levels increase the incidence of prostate cancer. Thus, DRE combined with PSA testing should be recommended for all men aged over 50 years or 45 years, once a year at risk populations to improve the rate of early detection PCa.

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Conflicts of interest

The authors declare no conflict of interest.

The contribution of the authors was effective during the study, drafting and correction of the article.

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