Meirelles RF Jr, Ceneviva R, Caboclo JLF, Eisenberg MM. Estudo das alterações do fluxo capilar pancreático após infusão de ceruleína avaliado por laser-Doppler em ratos. Acta Cir Bras [serial online] 2003 vol 18 suppl 5. Disponível em www.scielo.br/acb.

RESUMO – Objetivo: O fluxo capilar pancreático (FCP) foi estudado para determinar suas alterações durante a pancreatite aguda induzida por ceruleína, em ratos. **Métodos:** Vinte ratos foram divididos em grupo controle e grupo ceruleína. Um laser-Doppler fluxímetro foi empregado para determinar, continuamente, o FCP durante 120 minutos. A pressão arterial média (PAM) e a freqüência cardíaca (FC) foram determinadas, durante o experimento. Análise bioquímica sérica e estudo histopatológico, por microscopia ótica, do tecido pancreático foram realizados, ao final do experimento. **Resultados:** O FCP foi em média 109,08 ± 2,17% e 68,24 ± 16,79% nos grupos controle e ceruleína , respectivamente. No grupo ceruleína, houve uma diminuição média de 31,75 ± 16,79%. Os níveis de amilase sérica foram de 1323,70 ± 239,10U.I^{-1} e 2184,60 ± 700,46U.I^{-1} nos grupos controle e ceruleína, respectivamente. Houve diferença significante ($p<0,05$) no FCP e na amilasemia, quando comparado o grupo controle com o grupo ceruleína. Embora micro e macrovacuolização estivessem presentes no grupo ceruleína, não houve diferença histológica entre os grupos. **Conclusão:** A diminuição do FCP parece um evento precoce, antecedendo o aparecimento de alterações histopatológicas, por microscopia ótica, que caracterizam este modelo de pancreatite edematosa aguda.

DESCRITORES: Fluxo sanguíneo. Ceruleína. Pancreatite. Laser-Doppler.

Correspondence to:
Dr. Roberto Ferreira Meirelles Junior
Faculdade de Medicina de São José do Rio Preto, S.P.
Departamento de Cirurgia
Av. Brigadeiro Faria Lima, 5544 Cep; 15090-000
São José do Rio Preto, S.P.
e-mail: rmeirelles.hbse@famerp.br

Free PSA and prostate volume on the diagnosis of prostate carcinoma[1]

Antonio Carlos Pereira Martins[2], Antonio Antunes Rodrigues Jr[3], Rodolfo Borges Reis[2], Tiago Borelli Bovo[4]
Haylton Jorge Suaid[2], Adauto José Cologna[2], Silvio Tucci Jr[2], Edson Luis Paschoalin[3]

Martins ACP, Rodríguez J AA, Reis RB, Bovo TB, Suaid HJ, Cologna AJ, Paschoalin EL. Free PSA and prostate volume on the diagnosis of prostate carcinoma. Acta Cir Bras [serial online] 2003 vol 18 suppl 5. Available in www.scielo.br/acb

ABSTRACT – Objective: To analyse the influence of prostate volume on the performance of total prostate specific antigen (tPSA) and free PSA (fPSA) on the diagnosis of prostate adenocarcinoma. **Methods:** A total of 188 patients underwent transrectal ultrasound guided biopsies (10-12 cores) due to prostate nodes detected by digital rectal examination and/or tPSA range of 2.5-10ng/ml. Mean age was 65.7±8.7 years. 19/100 (19%)(GI) patients with prostate volume >40ml had prostate cancer while the corresponding figure for patients with prostate <40ml was 26/88 (29.5%)(GII). We analyzed the sensitivity and specificity of tPSA at cut-off points of 2.5 and 4ng/ml as well as the influence of the ratio f/tPSA in both groups of patients. **Results:** In the group GI tPSA sensitivity and specificity were 94.4% and 19.5% at the cut-off level of 4ng/ml and 100% and 6% at 2.5ng/ml. The corresponding values for GII were 76.5% and 62.9%, and 100% and 19.3%. In group GI a cut-off of 19% for the ratio f/tPSA kept tPSA sensitivity over 90% while the specificity increased to 46.2% at cut-off level of 4ng/ml and to 32.9% at 2.5ng/ml. In the group GII the ratio f/tPSA was not able to increase the specificity of tPSA at a cut-off level of 4ng/ml without an expressive reduction of sensitivity. On the other side, for this group a cut-off of 16% for the f/tPSA ratio rose the specificity to 46.7% for a sensitivity over 90%. **Conclusion:** We recommend stratification of patients according to prostate volume to define tPSA cut-off point. The cut-off level of 2.5ng/ml for tPSA combined with f/tPSA ratio of 19% in prostates >40ml and 16% in prostates <40ml was a better option for prostate biopsy indication than tPSA at a cut-off of 4ng/ml associated or not with f/tPSA ratio.

KEY WORDS: Prostate specific antigen. Prostate. Carcinoma. Adenocarcinoma. Screening.

INTRODUCTION

The prostate specific antigen (PSA) is a kallicrein controlled by a gene on cromossome 19. It is a glicoprotein produced by the prostate epithelium which fuction is to promote semen liquefation[1,2]. In the plasma PSA circulates free or complexed with proteins: a1-antichemotrypsin (ACT) and a2-macroglobulin (MG). There are several types of assay to determine PSA level in the serum and the most common are able to measure the total PSA (tPSA) and the free PSA (fPSA).

Approximately 30% of the patients with tPSA between 4-10ng/ml bear prostate adenocarcinoma while 20% of tumors occur in

1. This research was developed at Hospital das Clínicas – FMRP-USP
2. Professor and Assistants of FMRP-USP
3. Post-graduation alumni of Department of Surgery – FMRP-USP
4. Medical resident of Hospital das Clínicas – FMRP-USP

patients with tPSA <4ng/ml[2,3,4,5]. In 1997, Catalona et al.[6] reported that 22% of patients with tPSA between 2.6 to 4ng/ml have prostate adenocarcinoma and that 80% of these tumors are confined into the gland. The digital rectal examination reveals no suspiction of prostate carcinoma in 96% of patients with tPSA between 2.5-4ng/ml[6,7]. Thus, there is a concern about the better tPSA cut-off level for biopsy indication that should be the one with the highest sensitivy and specificity. The use of a cut-off level of 2.5ng/ml is associated with a low specificity which could be increased by the combination of tPSA with f/tPSA ratio[7].

As benign prostate hyperplasia (BPH) increases tPSA level the prostate volume may affect the performance of the test, and for such reason the tPSA density might improve the specificity of the test without affecting its sensitivity[8]. On the other hand, there are reports suggesting that f/tPSA ratio is also influenced by prostate volume[9,10].

The aim of our study is to investigate the influence of prostate volume on tPSA performance and explore whether f/tPSA can enhance the test specificity.

METHODS

From February of 2002 to March of 2003, 188 men underwent transrectal ultrasound guided biopsies (10-12 cores) due to prostatic nodes detected by digital rectal examination and/or serum tPSA of 2.5 – 10ng/ml. The prostate volume was determined by transrectal ultrasound during the biopsy procedure. The mean age of the patients was 65.7±8.7 years. Of 100 men with prostates >40ml (GI), 19 (19%) had cancer. The proportion of prostate adenocarcinoma in men with prostate <40ml (GII) was 26/88 (29.5%). We analyzed the tPSA sensitivity and specificity at cut-off levels of 2.5 and 4.0ng/ml in both groups of patients and studied the influence of f/tPSA ratio on such parameters. The dosage of PSA was undertaken with kits from DPC-Immulite™.

The comparison of prevalence of carcinoma in prostates larger or smaller than 40ml according to tPSA range was performed by the two tail Fisher's exact test using a software Instat, version 3.0. The level of significance considered was 5%.

RESULTS

No patients in this series with tPSA below 2.5ng/ml had prostate cancer. The prevalence of tumor in the entire sample with tPSA between 2.5-4ng/ml was 17.3% (9/52) and 4-10ng/ml was 29.0% (36/124)(p=0.13). In patients with prostate volume <40ml (GII) tumor prevalence in the tPSA range of 2.5-4ng/ml and 4-10ng/ml was respectively 20.5% (7/34) and 45.2% (19/42). In prostates >40ml (GI) the respective proportions were 12.5% (2/18) and 20.7% (17/82). The prevalence of tumor in tPSA range 2.5-4ng/ml in prostates <40ml (7/34) was similar to that observed in prostates >40ml (2/18) (p=0.4). This comparison in tPSA range of 4-10ng/ml exhibited equivalent results (p=0.15).

The results of tPSA sensitivity and specificity are exhibited in Table 1. The level of 19% for f/tPSA was determined through the receiver operating curve as the best cut-off point for all groups, except for the GII at a tPSA cut-off level of 2.5ng/ml in which the best cut-off point was 16%.

DISCUSSION

Our data show that the prevalence of tumor in patients with tPSA between 2.5-4ng/ml is 17.3% which is quite impressive even though a bit lower than reported elsewhere[8,11]. In fact in our series such a proportion was similar to that observed in cases with tPSA of 4-10ng/ml (p=0.13).

The sensitivity and specificity of tPSA at a cut-off of 4ng/ml for the entire sample are within the range published elsewhere[3,4,12]. However, it is important to stress that at this cut-off point a large proportion of tumors is missed inasmuch as if one associates the f/tPSA ratio under 19% to make a decision to indicate or not the biopsy.

TABLE 1: Performance of tPSA associated of not to f/tPSA ratio.

PATIENTS	tPSA			tPSA + f/tPSA at 19%				
	cut-off ng/ml	Ss %	Sp %	Ss %	Sp %	Increase %Sp	B/T	MT %
All	2.5	100	11.8	**>80**	27.7	15.9	3.4	4.5
	4.0	84	38.1	**>90**	54.8	16.7	2.4	18.1
GI (>40ml)	2.5	100	6	**>90**	32.9	4.2	4.2	5.6
	4.0	94.4	19.5	**>90**	46.2	26.7	3.7	11.1
GII (<40ml)	2.5	100	19.3	**>90**	32.2	12.9	2.6	4.9
				>90	46.7*	14.5*	2.3*	7.7*
	4.0	76.9	62.9	**>70**	66.1	3.2	2.0	23

Ss – sensitivity, Sp – specificity, * – cut-off f/tPSA at 16%, B/T – number of biopsies per tumor, MT – missed tumor

As reported previously[6,7,12] a tPSA cut-off of 2.5ng/ml for all patients exhibits a low specificity which means a low yield prostatic biopsies. It is also interesting to notice in Table 1 that prostate volume affect the test performance in both cut-off levels as described by others[12,13]. A possible reason to explain such influence is the lack of a regular pattern of tissue composition seen in BPH which is responsible for the increase of prostate volume. The proportion of glands is usually higher in benign prostates >40ml which affects tPSA density as well as the ratio of free-to-total PSA[9,12,13].

The sensitivity of tPSA is high and the specificity is low in both cut-off levels for prostates >40ml. A cut-off point of 19% for f/tPSA ratio was able to enhance expressively the specificity of the test in both cut-off levels in this group of patients (GI). It is worth to mention, however, that the adoption of this additional parameter to indicate the biopsy increases the proportion of missed tumor to 5.6% or 11.1% respectively for the tPSA cut-off of 2.5 or 4.0ng/ml.

Some authors proposed a cut-off point of tPSA that increases with age range to avoid unnecessary biopsies[14,15]. As a matter of fact, such proposal reflects indirectely the prostate growth with aging in consequence of BPH. But, it is known that nearly 15 to 20% of elderly men have prostates of normal size, which makes the proposal imprecise. On the other side, there are men in the fifties with larger prostates than the usual. In our series, adenocarcinoma occurred in 45.2% of the prostates smaller than 40ml and tPSA higher than 4ng/ml. It is unwise to avoid biopsies in such patients. Perhaps, patients should be stratified according to prostate volume to define tPSA cut-off point instead of age-range. For men with prostates <40ml a tPSA cut-off of 2.5ng/ml combined with a f/tPSA ratio of 16% represented a better option than the cut-off of 4ng/ml. It is worth to mention that the most convincing recent report, involving the screening and follow-up of 12,902 men, showed that the 95% percentile of tPSA was 2.45ng/ml for men without adenocarcinoma, and for this reason such value was proposed as the upper limit of normality[16].

CONCLUSION

We recommend stratification of patients according to prostate volume to define tPSA cut-off point. The cut-off level of 2.5ng/ml for tPSA combined with f/tPSA ratio of 19% in prostates >40ml and 16% in prostates <40ml was a better option for prostate biopsy indication than tPSA at a cut-off of 4ng/ml associated or not with f/tPSA ratio.

REFERENCES

1. Palooka TJ, Osterling JE, Partin AW. Prostate specific antigen: a decade of discovery – what we have learned and where are going. J Urol 1999; 162: 293-306.
2. Stamey TA, Kabalin JN. Prostate specific antigen in the diagnosis and treatment of adenocarcinoma of the prostate. I. Untreated patients. J Urol 1989; 141: 1070-5.
3. Catalona WJ, Smith DS, Ratliff TL, Dodds KM, Coplen DE, Yuan JJ, Petros JA, Andreole GL. Measurement of PSA in serum as screening test for prostate cancer. N Engl J Med 1991; 1156-61.
4. Brawer MK, Chetner MP, Beatie J, Buchner DM, Vessella RL, Lange PH. Screening for prostatic carcinoma with prostate specific antigen. J Urol 1992; 147: 841-5.

5. Stephans C, Jung K, Diamandis PE, Rithtenhouse HG, Lein M, Loening AS. Prostate specific antigen, its molecular forms, and other kallikrein markers for detection of prostate cancer. Urology 2002; 59: 2-8.
6. Catalona WJ, Smith DS, Ornstein DK. Prostate cancer detection in men with serum PSA concentrations of 2.6 to 4.0ng/ml and benign prostate examination. Enhancement of specificity with free PSA measurements. JAMA 1997; 277: 1452-6.
7. Catalona WJ, Partin AW, Finlay JA, Chan DW, Rittenhouse HG, Wolfert RL, Woodrum DL. Use of percentage of free prostatic-specific antigen to identify men at high risk of prostate cancer when PSA levels are 2.51 to 4.0ng/ml and digital rectal examination is not suspicious of cancer: an alternative model. Urology 1999; 220-4.
8. Littrup PJ, Kane RA, Metlin CJ, Murphy GP, Lee F, Toi A, Badalament R, Babaian RJ. Cost-effective prostate cancer detection: reduction of low yield biopsies. Cancer 1994; 74: 3146-58.
9. Okihara K, Fritsche HA, Ayala A, Johnston DA, Allard WJ, Babaian RJ. Can complexed prostate specific antigen and prostatic volume enhance prostate cancer detection in men with total prostate specific antigen between 2.5 and 4.0ng/ml. J Urol 2001; 165: 193-6.
10. Haese A, Graefen M, Noldus J, Hammerer P, Huland E, Huland H. Prostatic volume and ratio of free-to-total prostate specific antigen in patients with prostatic cancer or benign prostatic hyperplasia. J Urol 1997; 2189-92.
11. Gann PJ, Hennekens CH, Stampfer MJ. A prospective evaluation of plasma prostate specific antigen for detection of prostatic cancer. JAMA 1995; 273: 289-94.
12. Martins ACP, Bovo TJB, Reis RB, Paschoalin EL, Cologna Aj, Suaid HJ. Performance of PSA and of PSA density in the diagnosis of prostate carcinoma. Acta Cir Bras 2002; 17(S): 7-11.
13. Stephans C, Lein M, Jung K, Rudolph B, Schnorr D, Loening SA. The influence of prostate volume on the ratio of free to total prostate specific antigen in serum of patients with prostate carcinoma and benign prostate hyperplasia. Cancer 1997; 79: 104-9.
14. Oesterling JE, Jacobsen SJ, Chute CG, Guess HA, Girman CJ, Panser LA, Lieber MM. Serum PSA in a community-based population of healthy men: establishment of age-specific reference range. JAMA 1993; 270: 860-4.
15. Richardson TD, Oesterling JE. Age-specific reference ranges for serum prostate-specific antigen. Urol Clin North Am 1997;24:339-51.
16. Cheli CD, Levine R, Cambetas DR, Kolker JD, Roberts SB. Age-related reference ranges for complexed prostate-specific antigen and complexed/total prostate-specific ratio: results from East Texas Medical Center Cancer Institute screening campaign.

Urology 2002; 60 (Suppl A): 53-9. Martins ACP, Rodríguez J AA, Reis RB, Bovo TB, Suaid HJ, Cologna AJ, Paschoalin EL. PSA livre e volume prostático no diagnóstico do cancer da próstata. Acta Cir Bras [serial online] 2003 vol 18 suppl 5. Disponível em www.scielo.br/acb

RESUMO – Objetivo: Investigar a influencia do volume prostático no desempenho do PSA total (tPSA) e livre (fPSA) no diagnóstico do adenocarcinoma prostático. **Métodos:** 188 patients foram submetidos à biópsias prostáticas guiadas por ultra-som trans-retal (10-12 fragmentos) por apresentarem toque retal alterado e/ou tPSA entre 2,5 e 10ng/ml. A idade média foi 65,7±8,7 anos. A prevalência do câncer foi de 19% (19/100) em pacientes com próstatas >40ml (GI) e 29,5% (26/88) naqueles com próstatas <40ml (GII). Analisamos a sensibilidade e a especificidade do tPSA em corte de 2,5ng/ml e 4ng/ml bem como a influência do fPSA nos dois grupos de pacientes. **Resultados:** No grupo GI a sensibilidade e a especificidade do tPSA foram de 94,4% e 19,5% no corte de 4ng/ml e 100% e 6% no corte de 2,5ng/ml. Para o grupo GII os valores correspondentes foram 76,5% e 62,9%, e 100% e 19,3%. No GI a aplicação da fração f/tPSA, corte de 19%, manteve a sensibilidade do teste acima de 90% e elevou a especificidade para 46,2% no corte de 4ng/ml e 32,9% no corte de 2,5ng/ml. No GII a fração f/tPSA não foi capaz de elevar a especificidade do tPSA sem afetar significativamente a sensibilidade. Porém, neste grupo o uso do quociente f/tPSA de 16% elevou a especificidade do tPSA, corte de 2,5ng/ml, para 46,7% para sensibilidade acima de 90%. **Conclusão:** Recomenda-se estratificar os pacientes segundo o volume prostático para definir o corte do tPSA. O tPSA no corte de 2,5ng/ml, associado ao f/TPSA de 19% em próstatas >40ml e de 16% para próstatas <40ml representou melhor opção para indicação de biópsia que o tPSA no corte de 4ng/ml associado ou não à fração f/tPSA.

DESCRITORES: Antígeno prostático específico. PSA, rastreamento. Câncer, próstata. Adenocarcinoma.

Correspondence address:
Antonio Carlos Pereira Martins
Hospital das Clínicas – Departamento de Cirurgia
Av. Bandeirantes, 3.900, 9º Andar
Ribeirão Preto, SP, CEP: 14048-900

9 – ARTIGO ORIGINAL

Efeito do cloridrato de oxibutinina na hiperatividade vesical conseqüente a cistite hemorrágica [1]

Mizuma, EK [2]; Takeshita, MS[3]; Haylton Jorge Suaid[4] Antonio Carlos Pereira Martins[5] Silvio Tucci Jr[6] Adaulto José Cologna[6] Gonçalves, MA[7].

Mizuma EK, Takeshita MS; Suaid HJ, Martins ACP, Tucci Jr S, Cologna AJ, Gonçalves MA. Efeito do cloridrato de oxibutinina na hiperatividade vesical conseqüente a cistite hemorrágica. Acta Cir Bras [serial online] 2003 vol 18 suppl 5. Disponível em www.scielo.br/acb.

RESUMO – Introdução: A oxibutinina atua como agente anticolinérgico que tem ação anti-muscarínica e, principalmente, ação antiespasmódica na musculatura lisa vesical. Assim, ela causa aumento da capacidade vesical e diminui a frequência miccional e bloqueia o estímulo inicial da micção. **Objetivo**: Verificar se a oxibutinina atua sobre a hiperatividade vesical causada pela cistite hemorrágica, dependente do óxido nítrico. **Métodos**: Foram estudados dois grupos de animais. O controle com 5 ratas e o experimental com 10 ratas, cujos pesos variaram entre 200g a 250g. A cistite hemorrágica foi provocada pela injeção intraperitoneal de ciclofosfamida 200mg/