

THE EFFECTS OF GRADED EXERCISE ON PROSTATE SPECIFIC MARKERS ACTIVITY AND REPRODUCTIVE HORMONAL PROFILES

A.Żebrowska, W.Pilis

Dept. of Physiology, Academy of Physical Education, Katowice, Poland

Abstract. To determine the effects of physical exercise on serum prostate specific antigen (PSA), prostate acid phosphatase (PAP), and hormone levels, a group of twelve patients with bacterial prostatitis and twelve healthy volunteers were examined before and after a graded physical exercise test. Our results indicate that incremental physical exercise leads to metabolic, hormonal and prostate markers changes; the effects are more pronounced in patients with prostate disease. The serum PSA concentration and PAP activity in both investigated groups during physical exercise test was different and proportional to exercise intensity. In patient group serum PSA concentrations depend on basal levels of circulating testosterone. *(Biol.Sport 21:93-102, 2004)*

Key words: Exercise - Prostate specific markers - Testosterone

Introduction

Both prostate specific antigen (PSA) and prostate acid phosphatase (PAP) are serum markers which are useful in early detection of prostate diseases, and especially of prostate cancer [12,17]. The main factors considered in prostate cancer are: prolonged androgenic stimulation, high intake of fat-derived calories [18,22], increase levels of circulating testosterone [24,26], and anabolic steroid supplementation [20,21].

It was observed that men who participate in vigorous physical activity might have lower levels of testosterone, which can protect subjects against prostate cancer [24]. There are no reports regarding the influence of the factors mentioned in the above section on other prostate diseases such as chronic bacterial prostatitis. It is evident that digital rectal examination, cystoscopy, biopsy and postoperative condition of a patient all influence serum PSA levels [16]. Stamey *et al.* [19] reported that the serum PSA level decreased in hospitalized inactive men while

Reprint request to: Dr Aleksandra Żebrowska, Dept. of Physiology, Academy of Physical Education, Mikołowska 72 a, 40-065 Katowice, Poland
Tel.: (032) 251 40 66; Fax: (032) 251 68 68; E-mail: zebr@awf.katowice.pl



physical exercise would enhance the activity of the enzyme. Leventhal *et al.* [9] confirmed that statistically significant difference existed between inpatient and outpatient serum PSA levels. However, graded exercise test caused no significant change in prostate markers levels [9]. The aim of the present study was to test whether graded physical exercise stimulates the secretion of prostate specific markers; and if any possible changes could be related to reproductive hormones concentrations.

Material and Methods

Subjects: Twelve healthy untrained men (group A) and twelve patients with chronic bacterial prostatitis (group B) participated in the study. All of them were free from medication for three months preceding the study. Before giving their voluntary consent to participate, the subjects were informed about procedures and possible risk involved. The studies were approved by the Ethics Committee of the Silesian School of Medicine in Katowice.

Subjects characteristics are summarized in Table 1.

Table 1

Basic characteristics of subjects ($\bar{x} \pm SD$); group A-healthy men (n=12); group B-patients with chronic bacterial prostatitis (n=12)

		Age (years)	Body mass (kg)	Height (cm)	BMI ($\text{kg} \cdot \text{m}^{-2}$)
Group A	\bar{x}	30.42	75.54	177.50	23.88
n=12	SD	2.35	10.40	5.34	2.59
Group B	\bar{x}	32.50	81.90	175.40	26.99
n=12	SD	3.42	5.90	5.77	2.17

Protocol: The subjects performed treadmill exercise test with graded increase initial running speed of $6 \text{ km} \cdot \text{h}^{-1}$ with increments of $2 \text{ km} \cdot \text{h}^{-1}$ every 3 minutes up to $12 \text{ km} \cdot \text{h}^{-1}$. The slope of the treadmill was constant (5°). At rest and in the third minute of each exercise load, blood samples were obtained from antecubital vein for the determination of prostate specific antigen (PSA) concentration and prostate acid phosphatase (PAP) activity. Moreover, small blood samples (0.05 ml) were drawn from finger tip for the determination of lactate concentration (LA). Additionally, in group B, concentration of such hormones as testosterone (T),



progesterone (PE), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) were determined. Heart rate (HR), pulmonary ventilation and oxygen consumption were also measured at rest and during exercise at the same time points as blood samples were taken.

Measurements: Beckman Measurement Chart was used for measuring oxygen consumption and pulmonary ventilation. Heart rate was continuously recorded using PE-3000 Sport-Tester (Polar Inc., Finland).

The concentrations of T, PE, FSH, LH were measured by radioimmunoassays. PSA was detected by chemiluminescence test, PAP activity by BIO-Merieux test while LA by enzymatic method using commercial kits (Boehringer, Mannheim, Germany).

Statistics: All data are means \pm SE. The unpaired Students t-test was used to detect statistical significance between groups. The relationship between enzymes activity was checked by Pearson correlation coefficient regression analysis. In each statistical analysis the level of significance was set at $P < 0.05$.

Results

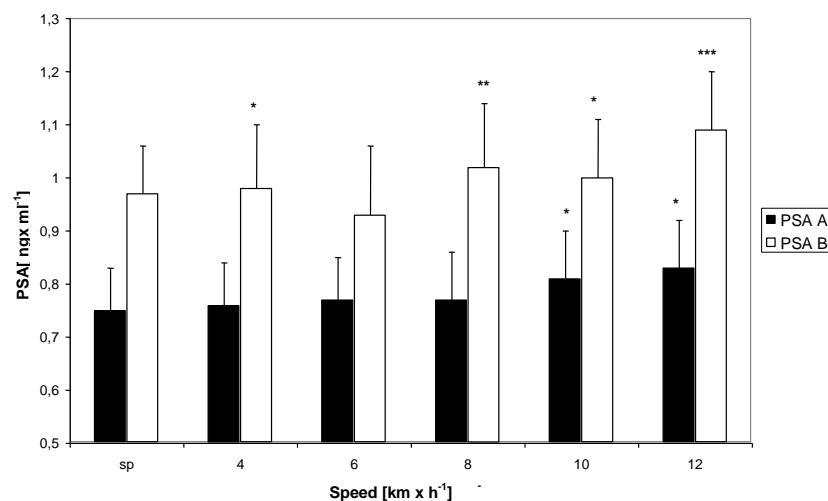


Fig. 1

Mean values (\pm SE) of prostate specific antigen (PSA) concentrations at rest and during graded physical exercise in healthy men (GR A) and patients (GR B) (*significant differences between rest and post-exercise concentration * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$)

There were no significant differences in mean serum concentrations of prostate specific antigen (PSA) between healthy men (Group A) and patients (Group B) (Fig. 1) whereas serum PAP activities were significantly higher in patients than in healthy men both at rest and at each treadmill speed (Fig. 2). The activities of both markers tended to be higher during exercise than at rest. Serum PSA concentration reached the level of statistical significance at a speed of 10 and 12 km·h⁻¹ in healthy men and at a speed of 4, 8, 10 and 12 km·h⁻¹ in patient group (Fig. 1).

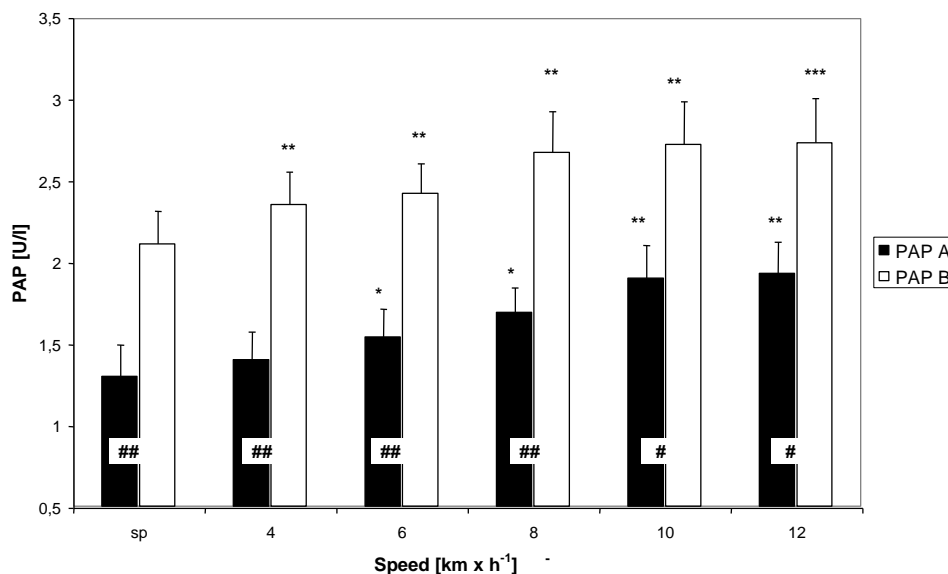


Fig. 2

Mean values (\pm SE) of prostate acid phosphatase (PAP) activities at rest and during graded physical exercise in healthy men (GR A) and patients (GR B)

*significant differences between rest and post-exercise concentration * $P < 0.05$;

** $P < 0.01$; *** $P < 0.001$;

#significant differences between both investigated groups # $P < 0.05$; ## $P < 0.01$

In comparison to rest values PAP activities were higher at each exercise speed in patient group, and at a speed of 6, 8, 10 and 12 km·h⁻¹ in healthy men (Fig. 2). Activities of both serum prostate enzymes correlated significantly only at rest. The correlation coefficients for healthy men reached $r = 0.76$ ($P < 0.01$), but in patient

group with chronic bacterial prostatitis this value was equal to $r=0.72$ ($P<0.01$). Moreover, a significant correlation was found at maximal exercise speed between PSA serum concentration and testosterone blood concentration in patients with chronic bacterial prostatitis ($r=-0.51$; $P<0.05$). There were no further correlations between blood hormone concentration and prostate function markers. Oxygen uptake was significantly higher in healthy subjects during very intensive exercise ($P<0.05$). Opposite pattern was observed at lower exercise intensities (Fig. 3).

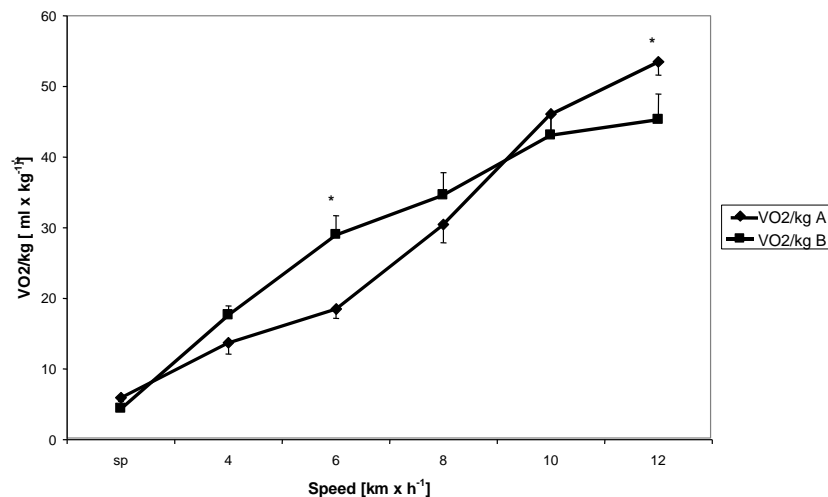


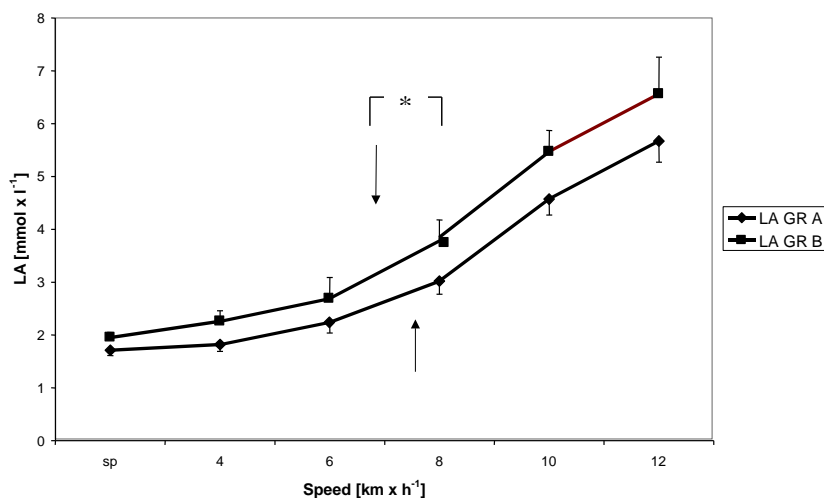
Fig. 3

Oxygen uptake in relation to body mass (VO_2/kg) during graded physical exercise in healthy men (GR A) and patients (GR B)

*significant differences between both investigated groups $*P<0.05$; $**P<0.01$; $***P<0.001$ (means \pm SE)

In both investigated groups blood lactate concentration (LA) showed an exponential pattern during graded exercise; this allowed us to calculate lactate threshold. In healthy subjects the threshold occurred at higher treadmill speed than in patients ($P<0.05$) (Fig. 4).



**Fig. 4**

Blood lactate concentration (LA) and lactate threshold during graded physical exercise in healthy men (GR A) and patients (GR B) significant differences between lactate threshold of both groups * $P < 0.05$ (means \pm SE)

Discussion

The results of our studies indicate that the concentration of PSA and the activity of PAP increased after physical exercise in the group of healthy subjects as well as in investigated patients with chronic bacterial prostatitis. It was observed that serum PSA concentration correlated to the running intensity on the treadmill, and also depended on the volume of the prostate. In addition we demonstrated the PSA and PAP concentrations were more pronounced in patients with chronic bacterial prostatitis in whom the prostate gland was enlarged. The quantity of prostate markers secreted into blood depends on prostate response to run-induced mechanical massage in this kind of physical exercise. As previously reported, mechanical pressure on the prostate during medical examination, e.g., digital rectal examination, causes an increase in the level of these markers [16,17,22,25]. Similar changes in the level of these antigens were detected in subjects after routine every day activity [1,13].

In the study of Leventhal *et al.* [9] changes in serum PSA concentration between inpatients and outpatients were significant, but exercise stress test had no

effect on the antigen. An opposite suggestion was made by Stamey *et al.* [19], who reported that physical exertion would cause an increase in serum PSA level. Dejter *et al.* [3] demonstrated no evidence of daily variability of these prostate markers in men.

In the light of such variation in serum concentrations of these markers, the use of serum PSA level for early diagnosis of prostate diseases should be considered controversial.

The higher activity of PAP, and the tendency to higher level of PSA in patients in comparison to healthy subjects is related to more intensive mechanical stimulation of the prostate during walking and running because of its enlargement. It was reported before, that serum PSA and PAP levels are indicators of prostate [2,10,17]. According to literature data significant correlation was found between both prostate markers in both groups examined, but only at rest. Our observations are in agreement with those of Stamey *et al.* [19], however the absence of such relationship during exercise is difficult to explain.

Additionally, an increase in serum PSA concentration and PAP activity was observed proportional to the increase in oxygen uptake and blood lactate concentration during physical exercise. It is well-known, serum PSA and PAP levels are not indices of exercise intensity. Higher values of oxygen uptake and lactate threshold in healthy subjects indicate greater physical capacity than in the case of patients with chronic bacterial prostatitis. Lower physical work capacity of patients is not a result of prostate disease, but rather a result of inactivity and sedentary work [20]. The patients in our study were not active physically. It is known that motivation to undertake physical effort is decreased in patients with prostate diseases [6] even if they are encouraged to engage in physical exercise [5,15].

There are numerous literature data regarding physical activity and prostate cancer [7,8,15]. One of the main reasons for increased risk of prostate diseases is enhanced serum testosterone level [11]. Paffenbarger *et al.* [14] and Wheeler *et al.* [23] reported that the post-exercise level of prostate markers depended on enhanced serum testosterone concentration. In our study this concentration was enhanced in the group of patients in comparison to its basal value, and correlated significantly with serum PSA level. This relationship was not observed at rest. As suggested before, post-exercise serum PSA and PAP level might be associated with mechanical prostate massage during running and walking. On the other hand, serum PSA enhancement is a well known effect of increasing serum testosterone concentration [2,4]. We do not know if these relationships exist in healthy subjects in whom we did not measure the concentration of these hormones. According to



literature data, trained athletes may have lower basal concentration of circulating testosterone than untrained men [20,23], which may result in lower risk of developing prostate cancer in athletes than in untrained subjects [7,8]. Basal concentration of testosterone might be more relevant to the risk of developing prostate cancer than sudden changes of this hormone which would occur after exercise. Whether physical activity decreases the risk of other prostate diseases, remains to be investigated.

Our results indicate that incremental physical exercise leads to changes in metabolism, hormone secretion and prostate markers levels. Some of these effects are more pronounced in patients with chronic bacterial prostatitis. The post-exercise changes of PSA and PAP levels are different and may depend on basal levels of circulating testosterone. Moreover, the physical performance of subjects with prostate diseases is lower than that of healthy men.

In conclusion, our results are in agreement with previous reports that physical exercise may cause clinically significant elevations in serum PSA concentration and PAP activity. We therefore conclude that, diagnostic blood sampling towards these prostate markers should not be performed after physical effort. The role of circulating blood testosterone in PSA and PAP level changes may be essential, however it requires further research.

References

1. Albanes D, A.Blair, P.R.Taylor (1989) Physical activity and risk of cancer in the NHANES 1 population. *Am.J.Publ.Health* 79:744-750
2. Arai Y, T.Yosiki, O.Yosida (1990) Prognostic significance of specific antigen in endocrine treatment for prostate cancer. *J.Urol.* 144:1415-1419
3. DeJter S.W., J.S.Martin, R.A.McPherson, J.H.Lynch (1988) Daily variability in human serum prostate-specific antigen and prostatic acid phosphatase: a comparative evaluation. *Urology* 32:288-292
4. Ghandian R., K.M.Push, E.M.Donoghue (1979) Serum testosterone and dihydrotestosterone in carcinoma of the prostate. *Br.J.Cancer* 39:696-699
5. Hartman T.J, D.Albanes, M.Rautalahti, J.A.Tangrea, J.Virtamo, R.Stolzenberg, P.R.Taylor (1998) Physical activity and prostate cancer in the Alpha-Tocopherol, Beta-Carotene (ATBC) Cancer Prevention Study (Finland). *CCC* 9:11-18
6. Lampman R.M. (1997) Exercise prescription for chronically ill patients. *Am.Fam.Physician* 1. 55:2185-2192
7. LeMarchand L., L.N.Kolonel, C.N.Yoshizawa (1991) Lifetime occupational physical activity and prostate cancer risk. *Am.J.Epidemiol.* 133:103-111
8. Lee I.M, R.S.Paffenbarger, C.C.Hsich (1992) Physical activity and risk of prostatic cancer among college alumni. *Am.J.Epidemiol.* 135:169-179



9. Leventhal E.K., T.A.Rozanski, A.F.Morey, V.Rholl (1993) The effects of exercise and activity on serum prostate specific antigen levels. *J.Urol.* 150:893-894
10. Lilja H., T.Bjork, P.Abrahamson (1994) Improved separation between normals, benign hyperplasia (BPH) and carcinoma of the prostate (CAP) by measuring free (F), complex (C) and total concentrations (T) of the prostate-specific antigen (PSA). *J.Urol.* 151:400
11. Nomura A., L.K.Heilbrun, G.N.Sremmermann et al. (1988) Prediagnostic serum hormones and the risk of prostate cancer. *Cancer Res.* 48:3515-3517
12. Oesterling J.K. (1991) Prostate specific antigen: a critical assessment of the most useful tumor marker for adenocarcinoma of the prostate. *J.Urol.* 145:907-923
13. Oremek G.M., U.B.Seiffert (1996) Physical activity release prostate-specific antigen (PSA) from the prostate gland into blood and increases serum PSA concentration. *Clin.Chem.* 42:691-695
14. Paffenbarger R.S, R.T.Hyde, A.L.Wing (1987) Physical activity and incidence of cancer in diverse populations: a preliminary report. *Am.J.Clin.Nutr.* 45:312-317
15. Pukkala E., J.Kapiro, M.Koskenvuo, U.Kujala, S.Sarna (2000) Cancer incidence among finnish world class male athletes. *Int.J.Sports Med.* 21:216-220
16. Rodriguez-Rubio F.J., I.E.Robles, A.Gonzales, J.Arocena, G.Sanz, F.Diez-Caballero, A.Martin-Marquina, J.M.Berian (1998) Effect of digital rectal examination and flexible cystoscopy on free and total prostate-specific antigen, and the percentage of free prostate-specific antigen. *Eur.Urol.* 33:255-260
17. Seamonds B., N.Yang, K.Anderson, B.Whitaker, L.M.Shaw, J.R. Bollinger (1986) Evaluation of prostate-specific antigen and prostatic phosphatase as prostate cancer markers. *Urology* 28:472-479
18. Severson R.K, A.Nomura, J.S.Grove, G.N.Stemmermann (1989) A prospective analysis of physical activity and cancer. *Am.J.Epidemiol.* 130:522-529
19. Stamey T.A., J.N.Kabalin (1989) Prostate-specific antigen in the diagnosis and treatment of adenocarcinoma of the prostate.I: Untreated patients. *J.Urol.* 141:1070-1075
20. Sternfeld B. (1992) Cancer and the protective effect of physical activity: The epidemiological evidence. *Med.Sci.Sports Exerc.* 24:1195-1209
21. Sutton J.R., M.J.Coleman, J.Casey (1973) Androgen responses during physical exercise. *Br.Med.J.* 1: 520-522
22. Tymchuk C.N., S.B.Tessler, W.J.Aronson, R.J.Barnard (1998) Effects of diet and exercise on insulin, sex hormone-globulin, and prostate-specific antigen. *Nutr.Cancer* 31:127-131
23. Wheeler G.D., S.R.Wall, A.N.Belcastro, D.C. Cumming (1984) The reduced serum testosterone and prolactin levels observed in male distance runners. *JAMA* 252:515-516
24. Yu H., R.E.Harris, E.L.Wynder (1988) Case-control study of prostate cancer of the prostate. *Cancer* 28:344-360



25. Yuan J.J., D.F.Coplen, J.E.Petros, R.S.Figenshau, T.L.Ratliff, D.S.Smith, W.J.Catalana (1992) Effects of rectal examination, prostate massage, ultrasonography and needle biopsy on serum prostate specific antigen levels. Part 2. *J.Urol.* 147:810

26. Zumoff B., J.Levin, G.W.Strain (1982) Abnormal levels of plasma hormones in men with prostate cancer: evidence toward a „two-disease theory”. *Prostate* 3:579-588

Accepted for publication 31.01.2002

