# ANNALES UNIVERSITATIS MARIE CURIE-SKŁODOWSKA LUBLIN-POLONIA 12.98 SECTIO D

**VOL. LVIII, N 2, 98** 

2003

Interfaculty Chair and Department of Public Health, Medical University of Lublin

### EDYTA OPALIŃSKA, ANNA MICHALAK, FILIP STOMA, MACIEJ LATALSKI, MARIUSZ GONIEWICZ

## Increasing level of prostate-specific antigen and prostate cancer risk factors among 193 men examined in screening procedure

Prevalence and mortality rates of prostate carcinoma, which is one of the most common cancers in men, are still increasing; however, the first studies indicating a little decline in a few countries have recently appeared (7). Prostate cancer has become an essential problem of public health, therefore some attempts have been undertaken to influence the disease development in its different stages. Primary prevention appears to be more important. To estimate the risk of the disease in population it is necessary to analyze prostate cancer risk factors. Among the factors influencing cancer development there are: androgens metabolism disorders, diabetes mellitus, overweight and obesity, smoking, alcohol and black coffee intake, diet rich in saturated fats and poor in unsaturated ones, lack of physical activity, geographical zone, race, and also such carcinogenic factors as: cadmium, substances used in rubber, painting, printing, ship industry, etc., and contagious factors like viruses (6). Older age, especially with a positive family history of prostate cancer, belongs to risk factors of the disease (4). To diagnose prostate cancer in its early stage such screening procedures are needed as physical examination – digital rectal exam (DRE) and determination of prostate-specific antigen (PSA) level in blood serum. Values of PSA assessed as normal vary in different age ranges; however, the usually accepted value in the majority of commonly-used tests and also accepted in that study is 4 ng/ml or less, values of PSA higher than 4 ng/ml suggest malignant process (13).

The aim of the study was to assess prostate cancer risk factors occurence among examined 193 men, determine PSA level in blood serum and examine correlation between them.

#### MATERIAL AND METHODS

Men – 193 subjects of over fifty years – reported to doctors at urology outpatient department at Clinical Hospital in Lublin suffering from urogenital disorders and for a routine control of the prostate gland. They filled in a questionnaire consisting of questions applying to personal data and 5 detailed ones about prostate cancer risk factors such as: saturated and unsaturated fats in a diet, black coffee intake, smoking, diabetes mellitus, overweight and obesity. The men were divided into 2 groups: 50–60 (younger) and over 60 years old (older). Smokers were separated into: smoking 1–10, 11–20 and over 20 cigarettes a day. Body mass index (BMI) defined as quotient of body mass in kilograms (kg) and height in square metres (m) was used to select men with normal BMI (<25 kg/m2) and risen BMI (>=25 kg/m2). Urogenital

symptoms were analysed, such as: diuria, nocturia, haematuria, disorders of urine stream, urgency to urinate, difficulty in passing or stopping of urine, defecation with miction, decrease of potency and others like weakness, lack of appetite, underbelly, crotch, low back pain or muscles pain (6). The questionnaire was completed with DRE and PSA measurement. All PSA determinations were made prior to any prostatic manipulations, including DRE. PSA results were divided into 2 ranges: normal (<=4 ng/ml) and risen (>4 ng/ml).

Statistical analysis performed by means of statistical programme STATISTICA 5.0.was based on non parametric chi square test (also with Yates correction) at a significance level of p<=0.05. No statistical significance was marked as NS.

#### RESULTS

The studied group included 193 men, aged 51–70, mean 59.3±5.9 years. According to the age they were divided into 59% of younger and 41% elders. The place of living was as follows: for 22.8% subjects – Lublin, for 19.8% – other towns, for 58% – rural area, and their marital status: 85% were married, 6.2% – widowers, 5.2% – divorced and 3.6% – single. Among the participants: 33.7% – had elementary education, 31.6% – vocational, 22.8% – secondary and 11.9% – higher education. Among working men a great percent (29%) worked in military service or police, 15% – in rubber industry, 9% – in painting industry, 5% – dealt with mechanical work. The other worked at schools, offices, in medicine, trading, printing industry, mining and agriculture. Of all: 41.6% – declared fat-riched diet, 65.8% – strong black coffee intake. Among 71%, who smoked cigarettes: 9.8% – smoked 1–10 cigarettes a day, 53.9% – 11–20 and 7.3% – over 20 items. Diabetes mellitus was diagnosed in 5.7%. BMI was found between 18.7 and 41.8, mean 27.4±3.9 kg/m2. In 29% of subjects BMI value was normal and in 71% – indicated overweight or obesity (Fig. 1).

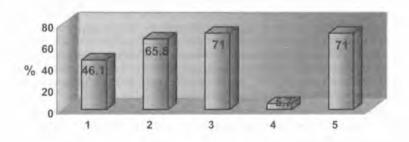


Fig. 1. Prostate cancer risk factors in the study; 1 – fat-riched diet, 2 – black coffee, 3 – smoking, 4 – diabetes mellitus, 5 – overweight and obesity

Respondents' complaints about urogenital symptoms involved: diuria (37.3%), nocturia (36.8%), urgency to urinate (26.4%), urine stream disorders (20.2%), difficulty in urinating (13.5%), stopping urine (5.2%), defecation during miction (4.7%), haematuria (2%) (Fig. 2). Additionally 45.6% of men suffered from decreasing potency, 18.1% – dryness in mounth, 23.3% - weakness, 7.8% – lack of appetite, 21.2% – underbelly or crotch ache, 19.2% – low back pain and 31.6% – muscles pain (Fig. 3). Percentage date do not need to be added because the respondents could report a few symptoms.

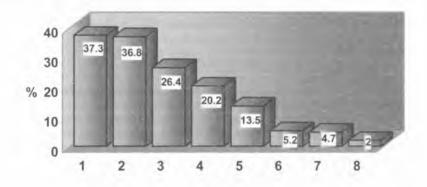


Fig 2. Reported urogenital symptoms; 1 – diuria, 2 – nocturia, 3 – urgency to urinate, 4 – urine stream disorders, 5 – difficulty in urinating, 6 – stopping urine, 7 – defecation during miction, 8 – haematuria

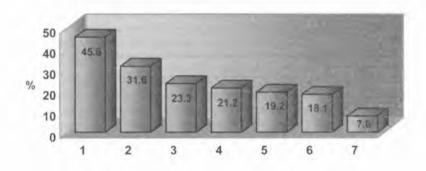


Fig 3. Reported other symptoms; 1- decrease of potency, 2- muscles pain, 3- weakness, 4- underbelly or crotch pain, 5- low back pain, 6- dryness in mounth, 7- lack of appetite

PSA level was between 1 and 10.56, mean 1.2±1,4 ng/ml. Of all the examined men: 96.9% – had normal PSA result and 3.1% – elevated over 4 ng/ml. Increased PSA level was found in 2.3% of inhabitants of Lublin, in 2.7% – of other towns and in 3.6% – of rural residence (NS). Elevated PSA was observed among 6.2% of men with elementary education, in 1.6% – with vocational and in 4.4% – with higher education (NS). Raised PSA result was received in 3% of married men and in 10% of divorced ones (NS). Elevated level of PSA was in 6.3% of elders and in 0.9% of younger ones (NS). Among men with raised PSA result there were twice more (66.7%) of those declaring a fat-riched diet than avoiding fatty products (33.3%) (NS). Among men with elevated PSA there were 50% of smoking 11–20 cigarettes a day and respectively 16.7% of smoking less than 10 and over 20 cigarettes daily and 16.6% of non-smokers (NS). Among those with raised PSA there were 83.3% of coffee drinkers and 16.7% of non-drinkers (NS). None of diabetic subjects had an increased PSA level (NS). Of the men with raised PSA there were twice more (66.7%) men with increased BMI than men with normal weight (33.3%).

Among those with raised PSA there were: 33.3% of men complaining of diuria (NS), 66.7% – nocturia (NS), 16.7% – difficulty to urinate (NS), 16.7% – stopping miction (NS), 16.7% – urine stream disorders (NS), 16.7% – decreasing of potency (NS), 16.7% – low back pain (NS).

### DISCUSSION

Prostate cancer is one of the most common cancers in men and the second leading cause of death among the male population. Because it develops with no symptoms or with just few in its early phase, it is often detected in its advanced stage, which means it is more difficult to treat. The aim of the screening procedures such as DRE and PSA test is to select men suspected of prostate cancer development. Following a number of advances in the management of prostate cancer, including introduction of the PSA test, there have been reports of declines in mortality in Canada, the United States, the United Kingdom, Austria, France and Germany over the period 1988–1991. It could have resulted from either reduction of prostate cancer risk factors in the population or uptake of PSA screening (9).

Data from population-based cohort study in Germany (8) including 11 644 men aged 45–75 years, who were examined by DRE and PSA, showed that in 82.8% of subjects PSA level was normal (<4 ng/ml), in 12.8% – elevated from 4 to 10 ng/ml and in 4.4% – raised than 10 ng/ml. Those percentage data were higher than in the authors' study, which could be connected with a different number of examined subjects and their various ranges of age. The German study also proved that a combination of both DRE and PSA was the most effective in the early detection of prostate cancer. In the study carried out in Urological Center in Perth, in eastern Australia (1) 211 men aged 50–79 years were examined by DRE and PSA. Elevated PSA result was detected in 9.5% participants, which is about three times higher than in the authors' study, but Australian research included a group of men 10-years older.

Prostate cancer risk factors presented in the questionnaire included: diabetes mellitus, overweight and obesity, smoking cigarettes, black coffee intake, diet riched in saturated fats and poor in unsaturated, old age, permanent contact with carcinogenic factors (6).

The correlation between the disease and diabetes mellitus is not certainly proved. According to some authors such a strong relationship exists - results of the study in Yugoslavia involving 101 patients with diagnosed prostate cancer and 202 healthy men as control group can be the example (5). On the other hand, the other study carried out on 100 000 American men, who were diagnosed as prostate carcinoma during 13-years follow up, found only slight correlation; however, the risk of the disease rose in men affected by diabetes mellitus at least 5 years (14). There were, however, other studies which even reported a protective influence of diabetes mellitus on prostate cancer incidence - in the analysis of 320 men with diabetes mellitus and prostate cancer from the medical university center in New York, compared to data obtained from 189 men with prostate cancer, non-diabetic, they found a lower risk of prostate cancer incidence in diabetic subjects; however, the effect would be probably lower in white male than in black ones (11). In the authors' study among men with elevated PSA there were only non-diabetic participants. Among those with raised PSA there were mainly smokers, especially smoking 11-20 cigarettes a day. Several findings showed a strong relationship between smoking and prostate cancer development - research from Canada (15) on the studied population of 1623 men with histologically diagnosed prostate cancer and a control group of 1623 healthy men confirmed a direct correlation: the greater number of daily smoked cigarettes and the length of the addiction, the more risk of prostate cancer incidence. In other studies they did not find such a relation (5,10). In the authors'own study among men with elevated PSA there was a majority of men using fat-rich diet. Some studies determined that excessive amounts of saturated fats in a diet, which consequently would lead to overweight or obesity, increased the risk of prostate carcinoma development - it was proved in the study of men in Iowa in the US (2) and in the research assessing the influence of typical Polish diet, which is rather rich in

fatty products, on the disease incidence (10). The effect is intensified by coexistence of increased BMI and smoking, which was proved by a comparison of the population including 399 men with diagnosed prostate cancer and 476 healthy men aged 45–70 years in Montreal in Canada (12). Older age, especially associated with family history of prostate carcinoma is considered to be an essential risk factor. Data from a population-based cohort study of 5706 Swedish men showed that both older age and close relatives with prostate cancer promoted prostate cancer development (4). In the authors' own study – elevated PSA appeared mainly in older men (>60 years old). Some carcinogenic factors were mentioned above. In the study quoted before, carried out in Yugoslavia (5), a direct correlation between prostate cancer incidence and those carcinogenic factors was proved. In the authors' own study such relation was not found.

Screening procedures using PSA test seem to be purposeful, which is proved in Physicians' Health Study carried out since 1982 on 22 000 men. From all the group there were selected 366 men with clinical symptoms of prostate cancer. After 10 years, in the blood samples taken before and stored, PSA level was determined. Prostate cancer did not appear only in 9% of the suspected men who had raised PSA level at the beginning of the study (3). In spite of many controversial opinions about the aim of screening procedures in prostate cancer detection, PSA test seems to be beneficial in early detection of prostate cancer, which would lead to a decline of the mortality rates.

#### CONCLUSIONS

- 1. In the studied population elevated PSA level is determined in 3.1% of 193 examined men.
- 2. Increased PSA occurs mainly in men from rural areas, with elementary education, divorced, older (>60 years), using fat-rich diet, smokers, black coffee drinkers, with overweight or obesity and non diabetic.
- 3. Combination of PSA test with DRE seems to be useful and rather cheap for the detection of prostate cancer in the early stage of its development.

#### **REFERENCES**

- 1. Brett T. D.: An analysis of digital rectal examination and serum-prostate-specific antigen in the early detection of prostate cancer in general practice. Fam Pract., 6, 529, 1998.
- Cerhan J. R. et al.: Association of smoking, body mass and physical activity with risk of
  prostate cancer in the Iowa 65+ Rural Health Study (United States). Cancer Causes &
  Control, 2, 229, 1997.
- 3. Gann P. H. et al.: A prospective evaluation of plasma prostate-specific antigen for detection of prostatic cancer. JAMA, 4, 289, 1995.
- 4. Gronberg H. et al.: Age specific risks of familial prostate carcinoma: a basis for screening recommendations in high risk populations. Cancer, 3, 477, 1999,
- 5. Ilic M. et al.: Case-control study of risk factors for prostate cancer. Br. J. Cancer, 10, 1682, 1996.) Wingo P. A., Tong T., Bolden S.: Cancer statistics, 1995. CA Cancer J. Clin., 45; 8, 1995.
- Leńko J.: Nowotwory gruczołu krokowego w Urologia t.II, red.: J. Zieliński, J. Leńko. PZWL 1993.
- 7. Littrup P. J. et al.: The benefit and cost of prostate cancer early detection. CA Cancer J. Clin., 43, 134, 1993.

- 8. Lubold H. J. et al.: Early detection of prostate cancer in Germany: a study using digital rectal examination and 4,0 ng/ml prostate-specific antigen as cutoff. Eur Urol., 2, 131, 2001.
- 9. Oliver S. E. et al.: International trends in prostate cancer mortality in the "PSA ERA". Int J Cancer, 6, 893, 2001.
- 10. Pawlęga J. et al.: Dietary factors and risk of prostate cancer in Poland. Results of case-control study. Neoplasma, 1, 61, 1996.
- 11. Rosenberg D. J. et al.: Diabetes mellitus and the risk of prostate cancer. Cancer Invest, 2, 157, 2002.
- 12. Sharpe C. R., Siemiatycki J.: Joint effects of smoking and body mass index on prostate cancer risk. Epidemiology, 5, 546, 2001.
- 13. Smith D. S. et al.: Longitudinal screening for prostate cancer with prostate-specific antigen. JAMA, 16, 1309, 1996.
- 14. Will J. C. et al.: Is diabetes mellitus associated with prostate cancer incidence and survival? Epidemiology, 3, 313, 1999.
- 15. Villeneueve P. J. et al.: Risk factors for prostate cancer: results from the Canadian National Enhanced Cancer Surveillance System. The Canadian Cancer Registries Epidemiology Research Group. Cancer Causes & Control, 5, 355, 1999.

#### **SUMMARY**

Prostate cancer is one of the most common cancers in men, therefore has become recently an essential problem of public health. The factors influencing cancer include: androgens metabolism disorders, diabetes mellitus, overweight and obesity, smoking, alcohol and black coffee intake, diet rich in saturated fats and poor in unsaturated, lack of physical activity, geographical zone, race, such carcinogenic substances as: cadmium, materials used in rubber, painting, printing, ship industry etc., contagious factors and also older age and a positive family history of the disease. To diagnose prostate cancer in its early stage such screening procedures as physical examination - digital rectal exam (DRE) and determination of prostate-specific antigen (PSA) level in blood serum are used. The aim of the study was to assess prostate cancer risk factors occurrence in the examined 193 men, aged 50-70 years, who reported to urology outpatient department at Clinical Hospital in Lublin, measure the PSA level in blood serum and examine the correlation between them. Respondents filled in a questionnaire about the presence of prostate cancer risk factors and urogenital symptoms. The questionnaire was completed with DRE and PSA measurement. The results led us to the following conclusions: 1/ in the studied population elevated PSA level is determined in 3.1% of 193 examined men, 2/ increased PSA occurs mainly in men from rural areas, with elementary education, divorced, older (>60 years), using fat-rich diet, smokers, black coffee drinkers, with overweight or obesity and non diabetic, 3/ a combination of PSA test with DRE seems to be useful and rather cheap for the detection of prostate cancer in the early stage of its development.

Podwyższony poziom specyficznego antygenu sterczowego w surowicy a obecność czynników ryzyka raka prostaty w badaniu przesiewowym 193 mężczyzn

Rak prostaty jest jednym z najczęściej występujących nowotworów wśród mężczyzn, co sprawia, że stał się obecnie istotnym problemem zdrowia publicznego. Do czynników ryzyka rozwoju choroby zalicza się: zaburzenia metabolizmu męskich hormonów płciowych, cukrzycę, nadwagę i otyłość, palenie papierosów, spożywanie alkoholu, mocnej kawy, dietę bogatotłuszczową, brak aktywności fizycznej, strefę geograficzną i rasę, występowanie czynników

karcynogennych w miejscu pracy, czynniki zakaźne oraz podeszły wiek i dodatni wywiad rodzinny w kierunku raka prostaty. Do wczesnego wykrycia nowotworu prostaty służa miedzy innymi badania przesiewowe, takie jak badanie fizykalne per rectum oraz oznaczenie specyficznego antygenu sterczowego w surowicy - PSA. Celem badania była ocena czestości występowania czynników ryzyka raka prostaty wśród grupy 193 mężczyzn w wieku 50-70 lat, którzy zgłosili się do Przyklinicznej Poradni Urologicznej przy Samodzielnym Publicznym Szpitalu Klinicznym nr 4 w Lublinie, oznaczenie poziomu PSA w surowicy krwi oraz ocena związku miedzy występowaniem czynników ryzyka choroby a podwyższonym poziomem PSA. Po wypełnieniu ankiety dotyczącej obecności czynników ryzyka nowotworu oraz dolegliwości ze strony układu moczowo-płciowego meżczyźni zostali poddani badaniu fizykalnemu (w tym per rectum). Z próbki pobranej krwi oznaczono PSA w surowicy. Uzyskane wyniki pozwoliły na sformułowanie następujących wniosków: 1) w badanej populacji lat nieprawidłowe wartości PSA stwierdza się u 3,1% badanych, 2) podwyższone wartości PSA występują przede wszystkim wśród meżczyzn mieszkających na wsi, posiadających wykształcenie podstawowe, rozwiedzionych, w wieku powyżej 60 lat, stosujących dietę bogatotłuszczową, palących, pijących mocną kawę, z nadwagą bądź otyłością, niechorujących na cukrzycę, 3) oznaczenie poziomu PSA w surowicy w połączeniu z badaniem fizykalnym gruczołu krokowego - per rectum, wydaje się użytecznym i stosunkowo tanim badaniem w celu wykrycia raka stercza we wczesnym stadium jego rozwoju.