Epidemiology of Prostate Cancer in the Mediterranean Population of Croatia – A Thirty-Three Years Retrospective Study

Josip Španjol[1], Anton Maričić[1], Tedi Cicvarić[2], Maksim Valenčić[1], Romano Oguić[1], Tomislav Tadin[2], Dora Fučkar[3] and Mirna Bobinac[4]

[1] Department of Urology, University Hospital of Rijeka, Rijeka, Croatia
[2] Department of Surgery, University Hospital of Rijeka, Rijeka, Croatia
[3] Department of Pathology, University Hospital of Rijeka, Rijeka, Croatia
[4] Clinic of Anesthesiology, University Hospital of Rijeka, Rijeka, Croatia

A B S T R A C T

Prostate cancer is a major public health problem of the male population in all the developed countries[1]. This non-skin cancer is the foremost one facing man today. Prostate cancer has become the second leading cause of cancer death[2]. In this study we investigated changes in the prostate carcinoma incidence and manifestation during a thirty-three years period. The study included 1,226 cases of prostate cancer diagnosed from 1972 to 2005 in the Primorsko-Goranska County, Croatia. The age-adjusted incidence of prostate cancer increased from 1.69 per 100,000 men annually in 1972 to 137.58 per 100,000 men annually in 2005, which is an 81.4-fold increase. The percentage of patients with bone metastases on the first medical examination decreased from 1972 (75%) to 2005 (15%). The most of the patients with bone metastases at the first medical examination were between 30 and 50 years old. Early detection measures, such as prostate specific antigen testing and transrectal ultrasound guided prostate biopsy combined with the raised public awareness of the disease, most probably resulted in an increase of incidence.

Key words: *prostate cancer, epidemiology, bone metastases, Croatia*

Introduction

Prostate cancer is a major public health problem of the male population in all the developed countries[1]. This non-skin cancer is the foremost one facing man today. Prostate cancer has become the second leading cause of cancer death[2]. Prostate cancer now outnumbers the lung cancer as the most common cancer in American men. The incidence of clinically detected prostate cancer is increasing in younger male patients[3].

Despite the recent progress made in molecular biology, the pathogenesis of prostate cancer remains poorly understood. The biological behavior of prostate cancer is highly unpredictable. While some patients die not from prostate cancer, others succumb rapidly to progressive disease[1,3]. The wide spectrum of biologic behavior exhibited by prostate cancer poses the difficulty of predicting the clinical course in the individual patient[1,4]. Attempts to reduce mortality have mainly focused on early detection of this disease currently based on three parameters: digital rectal examination (DRE), serum prostate-specific antigen (PSA) and transrectal ultrasound of the prostate (TRUS), although TRUS is mainly used as a guide for prostate biopsies[1–5].

With the advent of PSA screening programs and increased public awareness of the disease, the incidence of prostate cancer has dramatically increased over the past decade[2,4–6].

The epidemiology of the prostate cancer differs depending on geographic location, race, economic status, health care, public awareness concerning the disease etc[4,7,8]. The lowest rates occur in the Far East and on the Indian subcontinent, whereas the highest in the Western Europe, Australia and the North America. Adjusting the

rates to age standard population the incidence rate for prostate carcinoma was approximately from 3/100,000 men annually in China to 187/100,000 in the United States and 378/100,000 in Jamaica where the population is of African descent[4,7,8]. We also know little about risk factors of the prostate cancer[1,4]. The first and the most important step for preventing prostate cancer and improve the survival after the diagnosis is to determine the cause, risk factors and risk behaviors. To accomplish this goal we need more detailed, long-term epidemiology studies of the prostate cancer from all over the world. In our study we will show how the epidemiology of prostate cancer changes during a 33 years period (between 1972 and 2005).

Materials and Methods

The study included 1,226 cases of prostate cancer diagnosed from 1972 to 2005 in the Primorsko-Goranska County, Croatia. Information used to identify prostate cancer cases were taken from 4 urologic consulting rooms and the Department of Urology medical records of the Rijeka University Hospital. We have examined the medical records of all 1,226 patients with prostate cancer. All the relevant data for each patient were stored in a computer database created using *Access 2002* application (Microsoft, USA).

Incidence rates for the Primorsko-Goranska County were computed using data from the 1971, 1981, 1991 and 2001 Croatian censuses[9]. Age adjustments were made using the European standard population[10]. Proportions of patients with metastases, asymptomatic and symptomatic patients were calculated yearly. Proportions of prostate cancer patients according to 3 age groups (30–50, 51–70 and 71–95 years old) were computed for 3 periods (1972–1984, 1985–1993 and 1994–2005). In the period between 1972 and 1984 transrectal ultrasonography and PSA measurements were not used as diagnostic procedures for prostate carcinoma patients. In the period between 1985 and 1993 TRUS, but not PSA, was used as a routine diagnostic method. In the third period (1994–2005) both TRUS and PSA were routinely used in diagnosing prostate cancer. Proportions of prostate cancer patients with metastases according to 3 age groups (30–50, 51–70 and 71–95 years old) were computed for the same 3 periods.

The University Hospital of Rijeka with its Department of Urology and 4 urologic consulting rooms is the only medical center providing health care for all urologic patients in the Primorsko-Goranska County.

Primorsko-goranska County (2001 population: 347,235) lies at the Croatian Adriatic coast 200 km east of Venice (Italy) with 75% of its population residing in Rijeka, the county seat. In 2001 the population had 49% men, of
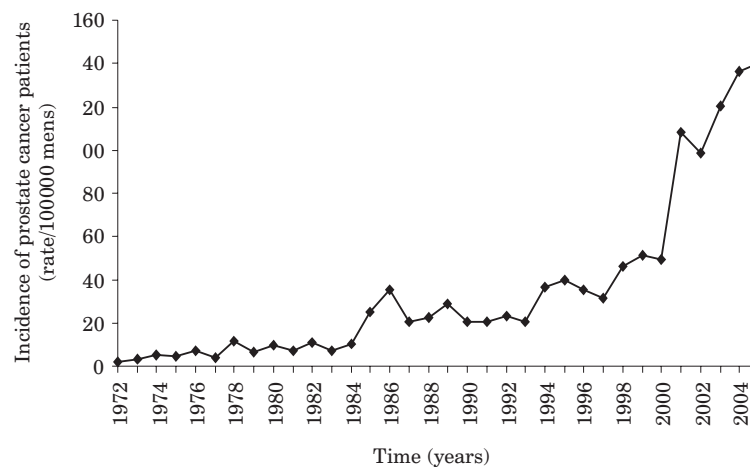

Fig. 1. Age-standardized incidence rate (European standard population) of prostate cancer patients in the Primorsko-Goranska County, from 1972 to 2005.
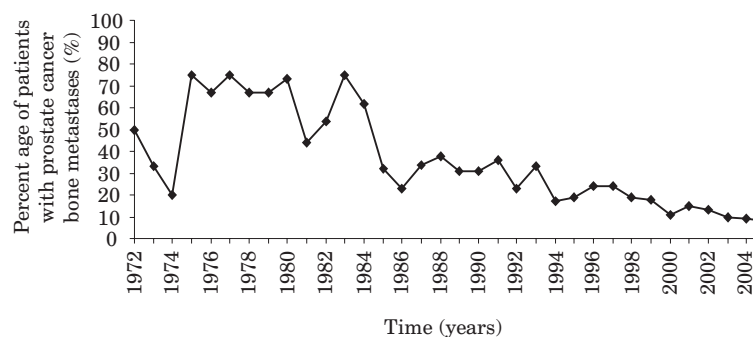

Fig. 2. Percentage of prostate cancer patients with bone metastases at the first medical examination, from 1972 to 2005.

whom 11% were over 65 years old. The population is largely middle class, with approximately 55% of the adult population having graduated from secondary school. The most of the economy is based on tertiary activities: tourism and transport[9].

Statistical analysis

Commercial software, Statistica 6.1 (StatSoft., Inc., Tulsa, OK, USA), was used for statistical analysis. Proportions ware compared statistically using either the χ^2 test or Fischer's exact test. The Mantel-Haenszel 1-degree of freedom correlation was used to test for the presence of a linear trend in proportions by year, $p < 0.05$ was considered statistically significant.

Results

There were 1,226 Primorsko-Goranska County men with the first diagnosis of prostate cancer made in the period from 1972 to 2005. The age-adjusted incidence of prostate cancer increased from 1.69 per 100,000 men annually in 1972 to 137.58 per 100,000 men annually in 2005, a 81.4-fold increase. There is a significant increase in prostate cancer incidence in 1985, 1994 and 2001 (Figure1). The percentage of patients with bone metastases at the first medical examination decreased from 1972 (75%) to 2005 (15%) ($p < 0.05$, Figure 2). The percentage of asymptomatic patients increased during the same period of time.

The highest percentage of patients with the first diagnosis of prostate cancer in the period from 1972 to 1984 was between 71 and 90 years old. The same relation remand in the period from 1985 to 1993. Between 1994 and 2005 the highest percentage of patients with prostate cancer was between 51 and 70 years old ($p < 0.05$, Figure 3).

In all three periods (1972–1984, 1985–1993, 1994–2005) the highest percentage of patients with bone metastases at the first medical examination was between 30 and 50 years old ($p < 0.05$, Figure 4).

The youngest patient with the first diagnosis of prostate cancer was 42 years old and the oldest one was 90 years old.

Discussion and Conclusion

Our results are clearly showing that the age adjusted incidence rate of prostate carcinoma patients was increasing during the period from 1972 to 2005. The percentage of prostate carcinoma patients with bone metastases at the first medical examination was decreasing during the same period of time (from 75% to 10%). The percentage of asymptomatic patients was increasing. We have also shown that the incidence of prostate carcinoma patients in the period from 1994 to 2005 was higher in the age group between 51 and 70 years, and in the periods from 1972 to 1984 and from 1985 to 1993 the incidence was higher in the age group between 71 and 90 years. In all the time periods that we have examined the
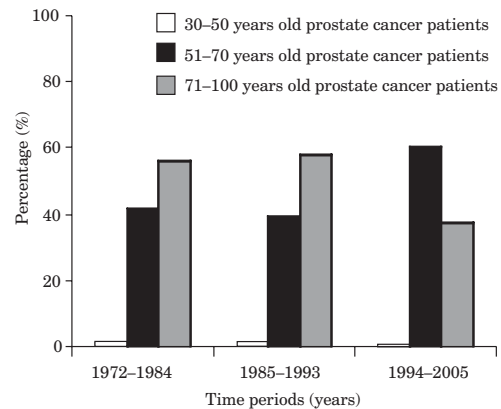

Fig. 3. Percentage of prostate carcinoma patients according to 3 time periods (1972–1984, 1985–1993 and 1994–2005) and 3 age groups (30–50, 51–70 and 71–90 years old).
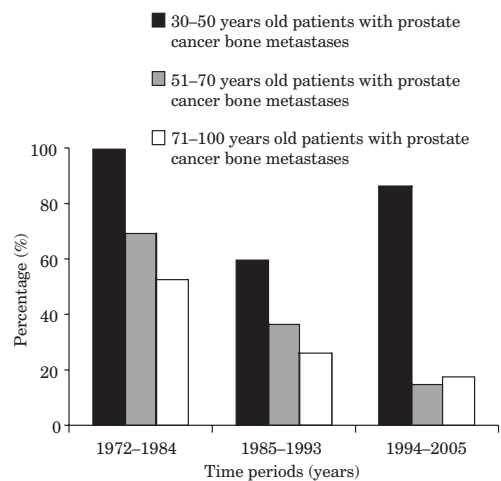

Fig. 4. Percentage of patients with bone metastases on the first medical examination according to 3 time periods (1972–1984, 1985–1993 and 1994–2005) and 3 age groups (30–50, 51–70 and 71–90 years old).

percentage of patients with bone metastases at the first medical examination was the highest in the youngest age group between 30 and 50 years. The increase of prostate carcinoma incidence during the examined 31 years can be mostly justified by the introduction of new diagnostic methods. The first significant increase of the incidence occurred in the 1985 with the beginning of TRUS use as diagnostic methods. The second increase occurred in the 1994 with the introduction of PSA measurement in the diagnostic algorithm. A similar finding was observed in the USA. The introduction of PSA testing in 1987 resulted in an enormous increase in the reported incidence of prostate cancer[3,6]. It is known that the PSA test detects prostate cancer at an early stage in many cases[3,4,6]. From 1987 the PSA has been increasingly used for diagnostic purposes[3,6]. At the beginning PSA was used in 5.1% and in 1994 in 60.6% of all newly diagnosed prostate carcinomas[3,6,7].

The raised public awareness of the disease in the community can also increase the incidence rate[3,4,6,7]. We have found very interesting and remarkable increase of the incidence occurring in 2001 and 2002. In those years we didn't introduce any new diagnostic methods. We have, however, performed in the collaboration with family doctors of the Primorsko-Goranska County a large action of informing 40 years and older men of the necessity of regular urological examinations (1 per year) in order to detect prostate cancer in early stage. The success of this action and a higher number of examinations in our consulting rooms were the most probable causes of this incidence increase.

There is wide variation in the incidence of prostate cancer around the world with a general raising pattern[3–8]. The incidence of prostate cancer in the southeast England has also increased markedly over the last 20 years[5].

In the Primorsko-Goranska County in the period from 1972 to 1993 about 60% of patients with newly diagnosed prostate carcinoma were between 71 and 90 years old. From 1994 to 2005 60% of patients were between 51 and 70 years old. The median age at the moment of diagnosing prostate cancer has been decreasing in the United States SEER registry since 1975[3,4,11]. In the southeast England the rising trend in incidence was seen in all age groups over 50 years. The decline has been mostly noticed in the older age groups from 1996[5]. We can speculate about two main reasons why the prostate cancer was diagnosed mostly in the younger age group in the last period of our study rather then in the previous two periods. In the period from 1994 to 2005 the common use of PSA made the diagnostic protocol more sensitive. Moreover the awareness of prostate cancer problem in general population was significantly higher. Therefore, the number of examinations in younger asymptomatic patients was higher.

The increased sensitivity of diagnostic protocol (TRUS and PSA) made possible to diagnose prostate carcinoma in its earlier stages, so the percentage of prostate carcinoma patients with bone metastases at the first medical examination was decreasing all through the years from 75% in 1972 to 10% in 2005.

The biological aggressiveness of prostate cancer diagnosed in younger patients resulted with the highest percentage of the bone metastases in the youngest age group between 30 and 50 years in all the three periods of time.

It is clear that the recorded incidence of prostate cancer is rising in many developed countries including Croatia. Early detection measures, such as prostate specific antigen testing and transrectal ultrasound guided prostate biopsy combined with the raised public awareness of the disease, have been shown to result most probably in an increase of incidence but also they caused the decrease of the median age at the moment of diagnosing prostate cancer and the decrease of the ratio of prostate carcinoma patients with bone metastases at the first medical examination. The biological aggressiveness of prostate cancer diagnosed in younger patients resulted with the highest percentage of the bone metastases in the youngest age group.

We still can't be certain that despite the apparent changes in incidence, the true disease occurrence remains the same. In order to respond and clarify this uncertainty further investigations and epidemiology monitoring of prostate cancer incidence should be performed.

REFERENCES

1. BONKHOFF H, Morphogenetic aspects of prostate cancer (Springer, Berlin, 2003). — 2. BARRY MJ, New En J Med, 344 (2001) 1373. — 3. JACOBSEN SJ, KATUSIC SK, BERGSTRALH EJ, OESTERLING JE, OHRT D, KLEE G, CHUTE CG, LIEBER MM, JAMA, 274 (1995) 1445. — 4. PLATZ EA, KANTOFF PW, GIOVANNUCCI E, Epidemiology of and risk factors for prostate cancer (Humana Press, Totowa, 2000). — 5. EVANS HS, MOELLER H, Eur Urol, 43 (2003) 337. — 6. LU-YAO GL, GREENBERG RE, Lancet, 343 (1994) 251. — 7. BOYLE P, GANDINI S, BAGLIETTO L, SEVERI G, ROBERTSON C, Eur Urol, 39 (2001) 2. — 8. GLOVER FE, COFFEY DS, DOUGLAS LL, CADOGAN M, RUSSEL H, TULLOCH T, BAKER TD, WAN RL, WALSH PC, J Urol, 159 (1998) 1984. — 9. DOKO H, Statistički ljetopis hrvatskih županija 2003 (in Croatian) (State Institute for Statistics, Zagreb, 2003). — 10. WATERHOUSE J, MUIR C, CORREA P, POWELL J, Cancer incidence in five continents (International Agency for Research on Cancer, Lyon, 1976). — 11. PERROTTI M, RABBANI F, FARKAS A, WARD SW, CUMMINGS KB, J Urol, 160 (1998) 811.

J. Španjol

Department of Urology, University Hospital of Rijeka, T. Strzica 3, 51000 Rijeka, Croatia
e-mail: jspanjol@vip.hr

EPIDEMIOLOGIJA KARCINOMA PROSTATE U MEDITERANSKOJ POPULACIJI HRVATSKE – TRIDESETTROGODIŠNJA RETROSPEKTIVNA STUDIJA

S A Ž E T A K

Karcinom prostate je vodeći javno-zdravstveni problem muške populacije u razvijenim zemljama[1]. Ovo je najčešći žljezdani rak u današnjeg muškarca. Karcinom prostate postao je drugi najčešći uzrok smrti među malignim bolestima[2]. U ovoj studiji proučili smo incidenciju i manifestaciju karcinoma prostate u razdoblju od protekle 33 godine. Studija je obuhvatila 1226 slučajeva karcinoma prostate dijagnosticiranih u razoblju od 1972 do 2005 godine u Primorsko-goranskoj županiji u Republici Hrvatskoj. Dobno prilagođena incidencija karcinoma prostate rasla je od 1.69 na 100000 muškaraca godišnje 1972. do 137.58 na 100000 muškaraca godišnje 2005 godine, što je porat od 81.4 puta. Postotak bolesnika s koštanim metastazama dijagnosticiranim kod prvog liječničkog pregleda pao je sa 75% (1972 godine) na 15% (2005 godine). Većina bolesnika s koštanim metastazama kod prvog pregleda bila je stara između 30 i 50 godina. Metode ranog otkrivanja, kao što je prostata specifični antigen i transrektalna, ultrazvukom vođena, iglena biopsija prostate u kombinaciji s povišenom razinom javne svijesti o nužnosti preventivnih pregleda, vjerojatni je uzrok povećanja incidencije karcinoma prostate.