Prostate Cancer Incidence and Mortality in Selected Countries of Central Europe

Incidencia a mortalita na karcinóm prostaty vo vybraných krajinách strednej Európy

Ondrusova M.1, Muzik J.2, Kliment J.3, Gulis G.4, Ondrus D.5

- ¹ Cancer Research Institute, Slovak Academy of Sciences, Bratislava, Slovak Republic
- ² Institute of Biostatistics and Analyses at the Faculty of Medicine and the Faculty of Science of the Masaryk University, Brno, Czech Republic
- ³ Department of Urology, Comenius University, Jessenius Faculty of Medicine, Martin, Slovak Republic
- ⁴Unit for Health Promotion Research, Institute of Public Health, University of Southern Denmark, Esbjerg, Denmark
- ⁵ 1st Department of Oncology, Comenius University, Faculty of Medicine, St. Elisabeth Cancer Institute, Bratislava, Slovak Republic

Summary

Backgrounds: This paper analyzes the incidence and mortality of prostate cancer in the Slovak (SR) and Czech (CR) Republics (as Central European countries with population-based cancer registries) before and after the introduction of PSA testing, the possible reasons for any differences disclosed, and compares the results with selected regions and countries around the world. Material, Methods and Results: In SR, the age-adjusted incidence of prostate cancer rose from 14.6/100,000 in 1968 to 36.2/100,000 in 2005. The estimated annual increase of incidence from 1968 to 1991 (before nation-wide PSA testing) was 0.421 and 1991–2003 it reached 0.941. The mortality rates rose from 7.3/100,000 in 1968 to 14.9/100,000 in 2005. The increase in incidence occurred faster in CR than in SR, from 15.8/100,000 in 1977 to 59.5/100,000 in 2005. The estimated annual increase of incidence in CR in 1977–1991 was 0.581, while in 1991–2003 it reached 1.981. Before 1991, mortality rose more sharply in CR than in SR while after the introduction of PSA testing mortality stabilized more quickly in the CR than in SR. In SR a significant reduction of mortality was observed after 2002 and is probably affected by more factors than those associated with the increase in PSA testing. Conclusion: The difference in the incidence and mortality of prostate cancer in SR and in CR results from a difference in the intensity of PSA testing as well as from the earlier introduction of effective treatment in CR.

Key words

cancer - incidence - mortality - prostate - PSA

Súhrn

Východiská: Predkladaná publikácia analyzuje incidenciu a mortalitu na karcinóm prostaty v Slovenskej republike (SR) a Českej republike (ČR) (predstaviteľov krajín strednej Európy s populačnými onkologickými registrami) pred a po zavedení vyšetrovania PSA, pátra po možných zdôvodneniach rozdielov ich vývoja a porovnáva výsledky s vybranými regiónmi a krajinami sveta. Materiál, metódy a výsledky: Štandardizovaná incidencia karcinómu prostaty v SR stúpla z hodnôt 14,6/100 000 v roku 1968 na 36,2/100 000 v roku 2005. Očakávaný ročný nárast incidencie bol v rokoch 1968–1991 (pred zavedením PSA vyšetrovania do klinickej praxe) 0,421, avšak v rokoch 1991–2003 už 0,941. Mortalita vzrástla z hodnôt 7,3/100 000 v roku 1968 na 14,9/100 000 v roku 2005. Incidencia rástla rýchlejšie v ČR ako v SR, z 15,8/100 000 v roku 1977 na 59,5/100 000 v roku 2005. Očakávaný ročný nárast incidencie v ČR v rokoch 1977–1991 bol 0,581, v rokoch 1991–2003 to bolo 1,981. Pred rokom 1991 mortalita rástla prudšie v ČR ako v SR, kým po zavedení vyšetrovania PSA sa rýchlejšie stabilizovala v ČR ako v SR. V SR sa významná redukcia mortality pozoruje až po roku 2002 a pravdepodobne nie je spôsobená len intenzívnejším vyšetrovaním PSA. Záver: Rozdiel v incidencii a mortalite na karcinóm prostaty v SR a v ČR je pravdepodobne výsledkom rozdielu v intenzite vyšetrovania PSA, ako aj skorším zavedením efektívnej liečby v ČR

splnil ICMJE kritéria pro publikace zasílané do biomedicínských časopisů.

The authors declare they have no potential

conflicts of interest concerning drugs,

Autoři deklarují, že v souvislosti s předmětem

The Editorial Board declares that the

manuscript met the ICMJE "uniform

Redakční rada potvrzuje, že rukopis práce

products, or services used in the study.

studie nemají žádné komerční zájmy.

requirements" for biomedical papers.

Martina Ondrusova, Dr, PhD.

Cancer Research Institute Slovak Academy of Sciences Vlarska 7 833 91 Bratislava Slovak Republic e-mail: Martina.Ondrusova@savba.sk

Submitted/Obdrženo: 15. 11. 2010 Accepted/Přijato: 15. 2. 2011

Kľúčové slová

karcinóm – incidencia – mortalita – prostata – PSA

Introduction

Prostate cancer is one of the most commonly diagnosed cancer in males. The 3% secular trend in the worldwide increase in the incidence is attributed to the steadily increasing life expectancy of the population especially in developed countries [1,2]. Latest estimates for 2008 indicate worldwide 903,452 new cases of prostate cancer (world standardized rates (hereafter WSR) of incidence 28.1/100,000), deaths number estimates in the same year are 258,381 (WSR mortality 7.5/100,000) [3].

The purpose of this study is to analyze the incidence of prostate cancer and resulting mortality and the possible reasons for any differences discovered in two neighboring countries in Central Europe (the Slovak and the Czech Republics) both of which have national, population-based cancer registries. When compared to the WSR incidence, the Slovak Republic (hereafter SR) with WSR of 36.2/100,000 and the Czech Republic (hereafter CR) with a WSR of

59.5/100,000 in 2005 [4] rank among European countries with a moderate incidence of the disease. However, when compared to the rates in Central and Eastern Europe the values are rather high. This paper compares the results of detected analyses of time progress of prostate cancer incidence and mortality in the CR and SR, discusses possible causal factors of their high incidence and compares the results with selected world countries.

Material and Methods

The data concerning the incidence of prostate cancer used in this analysis were obtained from the preprocessed data portals of the National cancer registry (hereafter the NCR) SR [5] (www.nor-sk.org) and the NCR CR [6] (www.svod.cz) valid until the end of July 2009 as well as from the standard outcomes and annual reports of the NCR SR and the NCR CR. These registries are national population-based cancer registries with high quality data [6]. The NCR

SR has been providing data on the incidence of cancer for the territory of the SR since 1968. The NCR CR has been providing population-based incidence data since 1977, the mortality values have been considered from NCR SR only after 1980, since the values for the years 1977-1979 were underreported. Corresponding national mortality data were obtained from the Statistical Office of the SR and from the NCR CR. The values of incidence and mortality are presented in the form of crude rates in the last statistically closed year 2005. The comparison with other countries is only possible after correction of different age structure in the population. The standardisation to the world standard population was performed [7] and the standardised rates in the CR and SR have been compared. The trends in incidence and mortality have been extracted using linear regression model separately for each country in time periods 1980-2003 and then individually the periods 1980-1991 and 1991-2003 and the trends are presen-

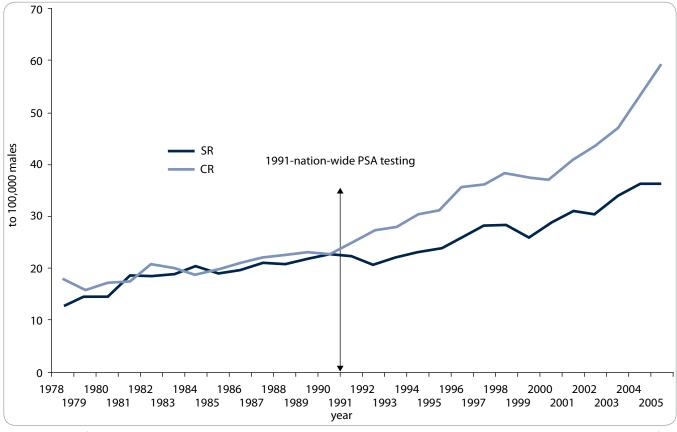


Fig. 1. Trends of age-adjusted (WSR) prostate cancer incidence in the Slovak Republic (SR) and the Czech Republic (CR) before (1980–1991) and after (1991–2005) nation-wide PSA testing.

ted with corresponding 95% Confidence Intervals (CI) and p-value with null hypothesis being constant with time. The year 1991 represents for both countries the year of the introduction of a nation-wide PSA testing, on that score the trends of incidence and mortality were compared not only for the entire period of 1980–2003, but also the character of their changes before and after PSA testing in 1991 was compared.

Results

In 2005, 1,264 cases of prostate cancer were diagnosed in the SR. This is a crude incidence rate of 48.3/100,000 and WSR incidence of 36.2/100,000 males [8]. Prostate cancer amounted to 9.7% of the total oncologic diseases in males, ranking 4th in the overall incidence of malignant tumors in males. In the analyzed time-period of 1968-2005, the incidence of prostate cancer in the SR grew long term, from a WSR 14.6/100,000 in 1968 (95% CI ± 1.5772) and 14.5/100,000 in 1980 (95% CI ± 1.4113) to 36.2/100,000 in 2005 (95% CI \pm 2.0678) (Fig. 1). This represents a 133.8% growth in the rate of incidence from the 1980 base. The estimated annual increase in the incidence of the disease during the period 1968-1991 was 0.421; from the year 1991 (when nation-wide PSA testing

began) up to 2003 (last year with valid data at the time of this analysis) it was 0.941.

The age-specific incidence in the SR exhibits a steep increase of incidence, especially in the age group 50 years and older. During the period 1999-2003, as many as 81.2% of prostate cancer patients in the SR were more than 65 years of age. However, when compared to the previous years, the risk of prostate cancer diagnosis increased by the same ratio in all age groups. No shift was observed towards the lower age groups as a result of the introduction of PSA testing in clinical practice. During the period 1978-1982, the percentage of prostate cancer cases in the 65+ age group was 83.3%. A small rise of incidence in the 75+ age group was observed from an average of 37.9% (272.89/100,000) in 1978-1982 to an average of 41.6% (533.66/100,000) during the period 1999-2003 (Fig. 2). During the period 1999-2003 the age-specific incidence rates were 0.1/100,000, 7.9/100,000, 68.4/100,000 and 246.8/100,000 respectively for age groups of 15-44, 45-54, 55-64 65+. The typical age of patients was between 65 (25% quantile) and 77 (75% quantile) years.

In 2005, 541 males died of prostate cancer in the SR, which represents

a crude mortality rate of 18/100,000 and a WSR of 14.9/100,000. Mortality values increased until 2002, but were slower than values for incidence. The rate of mortality rose from 7.3/100,000 in 1968 through 11.4/100,000 in 1980 up to 18.4/100,000 in 2005 (Fig. 3). This represents a 61.4% increase from 1980. During 1968-1991 the estimated annual increase in mortality was 0.285 but after 1991 mortality grew more slowly, i.e. by 0.253. The introduction of PSA testing in clinical practice was one of the factors responsible for slowing down the increase in mortality. Since 2002 there was a decrease of mortality observed in the SR that remained stable until 2008, the last year of processed data. It is assumed that alongside PSA testing the reduction in mortality can be ascribed to more efficient (hormonal) treatment during the 5-7 years prior before the observed reduction in mortality.

Age-specific mortality values increase with the increasing age of the patients. During the period 1999–2003 an average of 87.6% of prostate cancer deaths occurred in the 65+ age group. In the 15–44 age group the age-specific mortality in the SR was only 0.065/100,000 in the period 1999–2003, 3.24/100,000 within the 45–54 age group, 24.1/100,000 within the 55–64 age group and

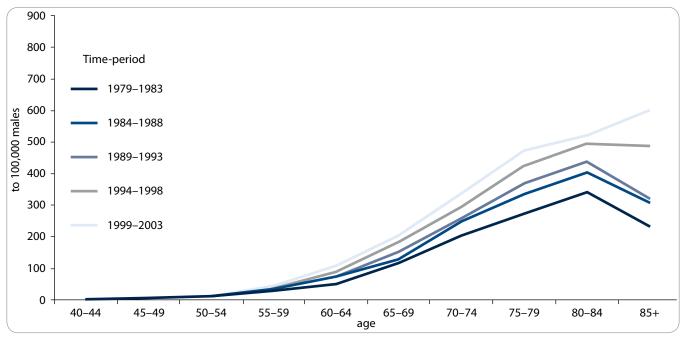


Fig. 2. Age-specific prostate cancer incidence in the Slovak Republic (SR) according to the defined time-periods.

286.53/100,000 within the 65+ age group. The age at the time of death was 69 years (25% quantile) to 81 years (75% quantile).

In 2005, 4,900 prostate cancer cases were diagnosed in the CR. This is a crude incidence of 98/100,000, and WSR incidence of 59.5/100,000 males. Prostate cancer was 13.5% of all malignant tumors in males, ranking 4th in the overall incidence of malignant tumors in males [6].

As in the SR, the CR observed a steady increase in the incidence of this malignant disease, slightly steeper in the CR compared to that in the SR (Fig. 1). Following the introduction of the PSA test during the early 1990s the increase in the incidence of the disease in the CR became more pronounced and increased more rapidly during recent years. In 1977 the WSR incidence in the CR was 15.8/100,000 (95% CI \pm 0.9748). However during the period of comparison with the SR, i.e. in 2003, the incidence was 46.8/100,000 (95% CI \pm 1.5520), representing an increase of 196.2%. The

estimated annual increase of incidence in the CR for 1977–1991 was 0.581. After 1991 (the beginning of the general PSA testing) and up to 2003, it was 1.981.

The age-specific incidence of prostate cancer in the CR shows characteristics that are very similar to those in the SR. A rapid rise of incidence occurs especially following the 5th decade of life, culminating in the oldest age groups. In the period of 1999-2003 an average of 79.9% of patients were 65 years or older at the time of diagnosis. Compared to the average age in the period 1978–1982 during which the 65+ age group comprised 83.6% of patients, this represents a slight shift in incidence of the disease towards younger age groups. This trend was not observed in the SR during the period under evaluation. However, similar to the SR there was no observation of a decrease in incidence in the highest age groups, i.e. 75+. During the period 1979–1983, 33.4% of the patients were in these age groups while during 1999-2003 it was 39.1% (Fig. 4). During the period 1999-2003 the average incidence of prostate cancer in the 15–44 age group was 0.2/100,000, in the age group 45–54 it was 12.4/100,000, in the 55–64 age group it was 112.1/100,000 and in the 65+ age group the age-specific incidence was 572.6/100,000 males.

In 2005, 1,430 patients died of prostate cancer in the CR, representing a crude mortality of 28.6/100,000 and a WSR of 16.4/100,000 males. In the CR mortality is shows a long-term increase. Before the introduction of PSA testing the increase was greater than in the SR, but following the introduction of PSA testing the increase is slower than in the SR. There was no observation of any significant mortality decrease during recent years, as observed in the SR (Fig. 3). The mortality (WSR) rose from 9.4/100,000 diagnosed in 1980 to 16.4/100,000 in 2005, i.e. a 74.4% increase in mortality. During the period of 1977–1991 the estimated annual increase of mortality was 0.882, after the introduction of PSA testing the increase was reduced to 0.342.

The age-specific mortality values rise sharply especially following the

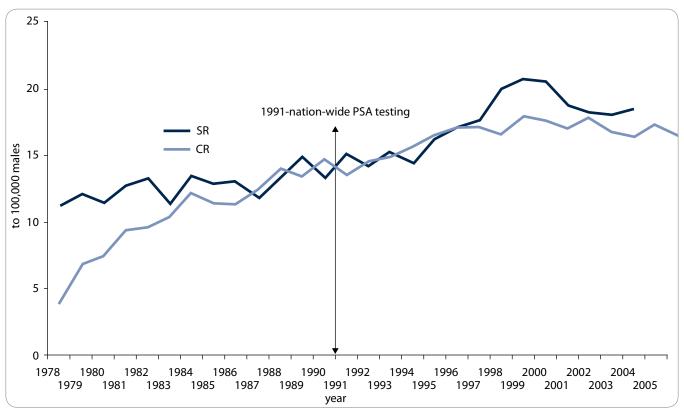


Fig. 3. Trends of age adjusted (WSR) prostate cancer mortality in the Slovak Republic (SR) and Czech Republic (CR) before (1968–1991) and after (1991–2005) nation-wide PSA testing.

6th decade of life. During the period of 1999–2003 an average of 89.8% deaths occurred in the 65+ age group. In the same period the average age-specific mortality in the CR in the 15–44 age group was 0.06/100,000 males, 2.6/100,000 in the 45–54 age group, 22.4/100,000 in the 55–64 age group and 365.7/100,000 in the 65+ age group. The typical age at the time of death was 71 (25% quantile) to 85 years (75% quantile).

Discussion

The incidence of prostate cancer varies greatly in individual geographic regions and countries of the world: the highest adjusted incidence rates are no more observed in the USA and in New Zealand, as it used to be in 2002 [3,7]. The highest incidence in 2008 is estimated to be in France (Martinique) (173.3/100,000) and in north European countries (Ireland 126.3/100,000, Norway 115.6/100,000, Sweden 114.2/100,000). In Australia and New Zealand the estimated incidence in 2008 was 104.2/100,000. In the USA, prostate cancer is accounting for an estimated 186,220 new cases in 2008 (WSR incidence 83.8/100,000 men) [3]. In Central and Eastern Europe the average incidence of prostate cancer in 2008 was estimated to be 28.5/100,000 (57,554 cases), in Northern Europe 75.2/100,000

(67,638 cases), in Southern Europe 50.2/100,000 (79,923 cases) and in Western Europe 94.1/100,000 (170,007 cases) [3].

With a WSR incidence of 36.2/100,000 (in the SR) [8] and 59.5/100,000 (in the CR) reported in 2005 [6], the SR and the CR are among European countries with a moderate incidence. One of the factors contributing to higher regional incidence in these two neighbor countries could be the fact that the cancer registries in the SR and the CR are among the most detailed and maintain the best quality in Central and Eastern Europe [7]. This fact is supported by a higher incidence in other European countries with good cancer registries [9]. In the Nordic countries mentioned above, prostate cancer incidence exceeds the incidence of lung cancer, a fact affected by the typical specific distribution of prostate cancer cases in the higher age groups and also by the aging population of these countries [1]. The lowest incidence of prostate cancer is estimated in several countries of the South-Central Asia (in average WSR 4.1/100,000) and China (4.3/100,000) [3]. A factor influencing the geographic distribution of prostate cancer is the variable degree in the utilization of the PSA exam and the ability to diagnose latent cancer. However, this is not the only reason. Even before 1980, i.e. before the PSA era, there was more than a 50-fold difference in the incidence of this disease worldwide [10,11].

In the SR PSA testing was introduced during the second half of the 1980s [12]. It likewise was introduced into the CR at the end of the 1980s and the beginning of the 1990s [13]. Nevertheless the WSR values for prostate cancer in both countries exhibited a slightly increasing trend with a sharper incidence beginning from 1991 (nation-wide use of PSA testing in both countries). The rising incidence is due mainly to the introduction of PSA testing in clinical practice. In the CR the WSR incidence rates are rising faster than in the SR. The rise of the WSR incidence in the SR (in 1980-2003) was 133.8% compared to 196.2% in the CR. So far, however, a temporary decline of incidence following the culmination of the increase, as seen in some countries that implemented the population screening [14,15] has not been observed in the two countries examined. This can be explained by a later introduction of the PSA test that was initially available only in dedicated centers. It is possible that the incidence rates will not culminate since the proportion of the population that is tested by PSA is still increa-

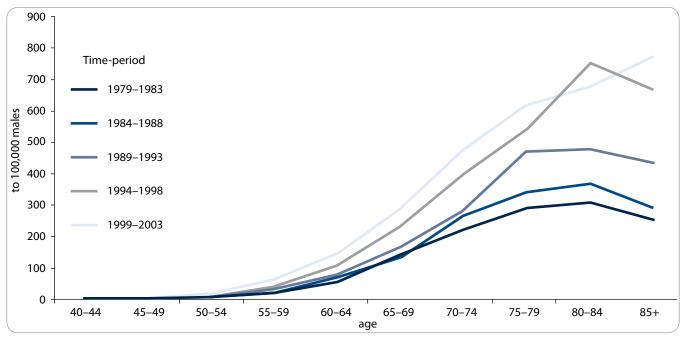


Fig. 4. Age-specific prostate cancer incidence in the Czech Republic (CR) according to the defined time-periods.

sing and nation-wide screening has not been implemented neither in the SR nor in the CR.

The difference between the age-adjusted incidence values for prostate cancer in the SR and in the CR can be explained mainly by the more extensive use of PSA test. This theory is supported by the fact that prior to the introduction of the PSA test the trend in incidence in both countries was approximately the same; following the introduction of PSA testing the increase in the average of incidence in the CR is more than double than in the SR. The more extensive use of PSA testing is also supported by the increase of disease in localized stages in CR and not in SR [6,5].

Interpretation of the risk factors influence in the SR and CR is not straightforward. For example the role of factors, such as obesity remains unclear despite the 34% higher risk of prostate cancer death for a very high BMI (35+kg/m²) compared with normal BMI as it was reported in the prospective Cancer Prevention Study [4]. Acording to the CINDI programme results in SR [16] in 1993-2002 it was reported the decrease of the number of males with overweight and obesity by 5.3%, however, there are no similar data on obesity prevalence development in CR to be compared with the situation and incidence time trends in SR. Even for factors that have been selected for rigorous testing in chemoprevention trials, such as selenium and vitamin E, there are no comparative data in both the countries.

The rate of prostate cancer mortality is increasing more slowly than the rate in the incidence of the disease. In some countries the rate has stabilized and even has tended to decline in recent years. At the same time differences among individual countries concerning mortality rate values are less pronounced when compared to the rate of incidence. This could be influenced by the method used to determine the cause of death from death certificates, especially of elderly males [17]. In Western Europe and in the USA the mortality rate culminated at the beginning of 1990s followed by a decline. In the EU, as a whole, prostate cancer mortality showed

a modest decline from 1990-1994 to 2000-2004 [18]. Declines were observed in the last decade in France, Germany and the UK, whereas prostate cancer mortality rates were still increasing in Russia, the Baltic countries, Poland and other central and eastern European countries [13,18,19]. This stabilized mortality and the increasing incidence can be partially explained by PSA testing that has resulted in the diagnosis of the disease at earlier stages of the disease that can be treated more effectively [13] and by the more radical treatment of localized, well differentiated tumors [20,21]. The age-adjusted mortality values in developed countries were 2.5-times higher (13.5/100,000) than those in developing countries (5.2/100,000). Reported mortality rates in the period studied ranged from 1.2/100,000 (Bangladesh) to 61.7/100,000 (Barbados) [3]. In 2002 prostate cancer was the cause of less than 1% of deaths from all causes in men and about 7% of deaths due to malignant disease [22]. In the CR the slowing down of the increase in mortality after the introduction of the PSA test was more pronounced than in the SR. The last years followed in the CR show that mortality has stabilized. After 2002 in the SR a decrease in mortality rates values was registered. Stabilized values have been maintained up to the present, assuming that there have been no systematic errors in the processing of national data. The quick decline in the mortality rate in the SR can be explained as a result of complex therapeutic management of prostate cancers shortly before changes are registered, especially by the improved treatment of the advanced stages of prostate cancer, that it does not seem possible to objectify unequivocally. It is probable that the use of the PSA test alone does not have such a marked influence upon the decline in the mortality rate since, according to the published data from the NCR SR, do not register increased numbers of localized illness (as compared to the situation in the CR where the number of cases in clinical stage II unequivocally increased according to the web portal www.svod.cz) [6] In so far as the decline in mortality is influenced by improved management of the treatment in advanced stages of the disease it concerns only a temporary state, post-poning the number of deaths until latter years. The development of mortality in the SR is being carefully monitored. As in several European countries (e. g. Sweden, France, Austria and England but also the SR and the CR), the decline in mortality rates that can be observed is probably the result of improved treatment of patients and higher survival rates [23].

The age-specific incidence curves generally demonstrate an exponential rise of incidence following the 5th decade of life. This trend is less pronounced in the Asian countries, but in western countries it represents the sharpest age-dependent rise among all malignant diseases [2]. A higher risk of death due to prostate cancer is associated with diagnosis at a younger age, African-American origins, and the advanced clinical stage of the disease. In countries where prostate cancer screening has been introduced, a shift of the age at the time of diagnosis towards lower age groups has been observed, resulting in the reduction of the median age of the patients; almost 37% of all diagnosed cases are in males younger than 65 years [14]. Unlike the SR, in the CR a shift of the age at the time of diagnosis towards lower age groups was observed, supporting the theory of more extensive PSA testing in the CR. The age-specific incidence curves for the SR and the CR are largely similar or identical with those in other developed European countries [7]. The incidence rises sharply after 50 years of age and culminates in the highest age groups.

Conclusion

Prostate cancer is one of the most frequently occurring malignant tumors in males, with the incidence increasing in western and more developed countries as a result of wide application PSA testing and developments in other diagnostic techniques. Following the introduction of PSA testing, the rise in incidence, previously similar in the CR and the SR, is two times higher in the CR than in the SR. The difference in the incidence of prostate cancer in the SR and CR is probably due mainly to the more extensive application of PSA testing in

the CR and corresponding higher rates of detection. The more extensive use of PSA testing is also supported by the increase of disease in localized stage in the CR and not in the SR. Prostate cancer mortality is slightly declining or stabilized in countries with an extensive use of PSA testing as a result of improved detection and earlier treatment. In the CR the mortality is rising even after the introduction of PSA testing although more slowly than before. In the SR the mortality rose faster than in the CR after the introduction of PSA testing. However after 2002 there was a sharp decrease in mortality rates that could be due to the introduction of more complex management and treatment of the advanced stages of the disease that delays mortality until later years. The results of this work point to a less extensive use of PSA testing in the SR and it is not clear whether the reduction of mortality in the SR will continue.

References

1. Boyle P, Severi G, Giles GG. The epidemiology of prostate cancer. Urol Clin North Am 2003: 30(2): 209–217.

- 2. Signorello LB, Adami HO. Prostate Cancer. In: Adami HO, Hunter D, Trichopoulos D (eds.) Textbook of cancer epidemiology. New York: Oxford University Press 2002: 400–428.
- 3. Ferlay J, Shin HR, Bray F et al. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. Lyon, IARC 2010. Available from: http://globocan.iarc.fr.
- **4.** Calle EE, Rodriguez C, Walker-Thurmond K et al. Overweight, obesity and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 2003; 348(17): 1625–1638.
- **5.** Ondrusova M, Plesko I, Safaei-Diba Ch et al. Comprehensive analysis of incidence and mortality of malignant tumours in the Slovak Republic. National Cancer Registry of the Slovak Republic, Bratislava, NHIC 2007. Available from: http://www.nor-sk.org/.
- **6.** Dusek L, Muzik J, Kubasek M et al. Epidemiology of Malignant Tumours in the Czech Republic. Brno, Masaryk University 2005. Available from: http://www.svod.cz.
- 7. Curado MP, Edwards B, Shin HR et al. Cancer Incidence in Five Continents. Vol. IX IARC Scientific Publications No. 160. Lyon: IARC 2007.
- **8.** Safaei-Diba Ch, Plesko I, Obsitnikova A et al. Cancer incidence in the Slovak Republic 2005. National Cancer Registry of the Slovak Republic. Bratislava: NHIC 2009.
- 9. Aareleid T. Central and Eastern Europe. In: Whelan SL (ed). IARC Newsletter No. 33. Lyon: IARC 2003.
- 10. Baade P, Youlden DR, Krnjacki LJ. International epidemiology of prostate cancer: geographical distribution and secular trends. Mol Nutr Food Res 2009; 53(2): 171–184.
- **11**. Haas GP, Delongchamps N, Brawley OW et al. The worldwide epidemiology of prostate cancer: perspectives from autopsy studies. Can J Urol 2008; 15(1): 3866–3871.
- **12.** Kausitz J. Use fo radioimmunoanalysis of tumor markers in diagnosis of carcinomas of the testes and prostate. Bratisl Lek Listy 1988; 89(10): 715–724.

- **13.** Kliment J, Ondrusova M, Abrahamova J et al. Epidemiology of malignant tumors of prostate comparison of the population of the CR and SR. Cesk Urol 2009; 13: 79–103.
- **14.** Horner MJ, Ries LA, Krapcho M et al. SEER Cancer Statistics Review, 1975–2006. Bethesda, NCI 2009. Available from: http://seer.cancer.gov/csr/1975-2006/.
- **15.** Levi F, Lucchini F, Negri E et al. Leveling of prostate cancer mortality in Western Europe. Prostate 2004; 60(1): 46–52
- **16.** Avdicova M. Report of CINDI (Countrywide integrated non-communicable disease intervention) programme feasance in Slovak Republic, 2002. Available from: www.vzbb.sk/sk/projekty/cindi_web.pdf.
- 17. Quinn M, Babb P. Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparison. BJU Int 2002; 90(2): 162–173.
- **18.** La Vecchia C, Bosetti C, Lucchini F et al. Cancer mortality in Europe, 2000–2004, and an overview of trends since 1975. Ann Oncol 2010; 21(6): 1323–1360.
- 19. Levi F, Lucchini F, Negri E et al. Trends in mortality from major cancers in the European Union, including acceding countries, in 2004. Cancer 2004; 101(12): 2843–2850.
- 20. Andriole GL, Crawford ED, Grubb RL 3rd et al. Mortality results from a randomized prostate-cancer screening trial. N Engl J Med 2009: 360(13): 1310–1319.
- 21. Hussain S, Gunnell D, Donovan J et al. Secular trends in prostate cancer mortality, incidence and treatment: England and Wales, 1975–2004. BJU Int 2008; 101(5): 547–555
- **22.** World Health Organization. The World Health Report 2004 Changing History. Geneva, WHO 2004.
- **23.** Hsing AW, Tsao L, Devesa SS. International trends and patterns of prostate cancer incidence and mortality. Int J Cancer 2000; 85(1): 60–67.