

Aim of the study: In Poland testicular tumours are the most frequent cancer among men aged 20–44 years. Testicular tumour incidence since the 1980s and 1990s has been diversified geographically, with an increased risk of mortality in Wielkopolska Province, which was highlighted at the turn of the 1980s and 1990s. The aim of the study was the comparative analysis of the tendencies in incidence and death rates due to malignant testicular tumours observed among men in Poland and in Wielkopolska Province.

Material and methods: Data from the National Cancer Registry were used for calculations. The incidence/mortality rates among men due to malignant testicular cancer as well as the tendencies in incidence/death ratio observed in Poland and Wielkopolska were established based on regression equation. The analysis was deepened by adopting the multiple linear regression model. A p -value < 0.05 was arbitrarily adopted as the criterion of statistical significance, and for multiple comparisons it was modified according to the Bonferroni adjustment to a value of $p < 0.0028$. Calculations were performed with the use of PQStat v1.4.8 package.

Results: The incidence of malignant testicular neoplasms observed among men in Poland and in Wielkopolska Province indicated a significant rising tendency. The multiple linear regression model confirmed that the year variable is a strong incidence forecast factor only within the territory of Poland. A corresponding analysis of mortality rates among men in Poland and in Wielkopolska Province did not show any statistically significant correlations.

Conclusions: Late diagnosis of Polish patients calls for undertaking appropriate educational activities that would facilitate earlier reporting of the patients, thus increasing their chances for recovery. Introducing preventive examinations in the regions of increased risk of testicular tumour may allow earlier diagnosis.

Key words: epidemiology, testicular tumours, incidence, mortality.

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Malignant testicular tumour incidence and mortality trends

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Introduction

Malignant testicular tumours belong to a group of rare neoplasms observed in men, constituting most frequently 1–1.5% of all malignant cancer diseases in this population [1–5]. They are, however, the most prevalent cancers among young men aged 15 to 45 years [2, 5–8].

More than 90% of all testicular tumours stem from germ cells (TGCT- testicular germ cell tumour), which may have the tissue of a pure seminoma (SEM – seminoma), a non-seminomatous tumour (NSGTC – non-seminomatous germ cell tumours), or belong to the mixed tumour type (MIX) [3, 7, 9, 10]. For this reason, the terms testicular tumour and testicular germ cell tumour are often used interchangeably [7].

In Poland testicular tumours constitute 1.6% of all malignant carcinomas in men, being the most frequent tumours among men aged 20–44 years [11]. Seventy-five per cent of such cases are seen in the age group 15 to 40 years [12]. The values of standardised malignant testicular cancer incidence rates in Poland towards the end of the 20th and in the first decade of the 21st century varied from 3.0 to 5.2/100,000, whereas the mortality rates ranged from 0.45 to 0.62/100,000. In the same period, incidence and mortality rates observed in Wielkopolska Province were higher (incidence ranging from 4.4 to 7.3/100,000, mortality from 0.44 to 1.2/100,000) [13]. The increased risk of mortality due to malignant sex-specific neoplasms, including testicular cancer, observed in the territory of Wielkopolska Province was emphasised already in the late 1980s/early 1990s [14].

Aim of the study

The aim of the study was the comparative analysis of the tendencies in incidence and death rates due to malignant testicular tumours observed among men in Poland and in Wielkopolska Province.

Material and methods

Data from the National Cancer Registry were used for calculations – crude rates and standardised incidence and mortality rates (direct standardisation method, using as standard the world standard population) due to testicular tumours observed among men in Poland and Wielkopolska Province in the period 1999–2011 [13]. Crude rates show the actual intensity of health-related problems without eliminating the effect of age on the value of those rates. Directly standardised rates bring the age structure of the two populations to the same pattern, giving an opportunity to compare the occurrence of diseases in different populations [14]. Directions of morbidity and mortality trends determined from the crude and standardised rates may vary.

Statistical methods

The incidence and mortality rates among men due to malignant testicular cancer as well as the tendencies in incidence/death ratio observed in Poland and in the territory of Wielkopolska were established based on regression equation. The analysis was deepened by adopting the multiple linear regression model, which tested an independent impact of the year on the value of incidence and mortality rates, i.e. after adjusting the age variable (as the confounding factor) as well as the interrelationship of age and year. A p -value < 0.05 was arbitrarily adopted as the criterion of statistical significance, and for multiple comparisons it was modified according to the Bonferroni adjustment to a value of $p < 0.0028$. Calculations were performed on the basis of PQStat v1.4.8 package.

Results

The incidence among men with malignant testicular neoplasms, calculated on the basis of crude and standardised rates, in the territory of Poland and Wielkopolska Province showed a significant rising trend, confirming a (recognised for this type of tumour) lack of correspondence between the rising incidence and the age of this population of men (Figs. 1, 2) [8, 12].

The line gradients (a), indicating the rate of growth, were similar for Poland and the Province of Wielkopolska (crude rates: $p = 0.6295$, standardised rates: $p = 0.5596$).

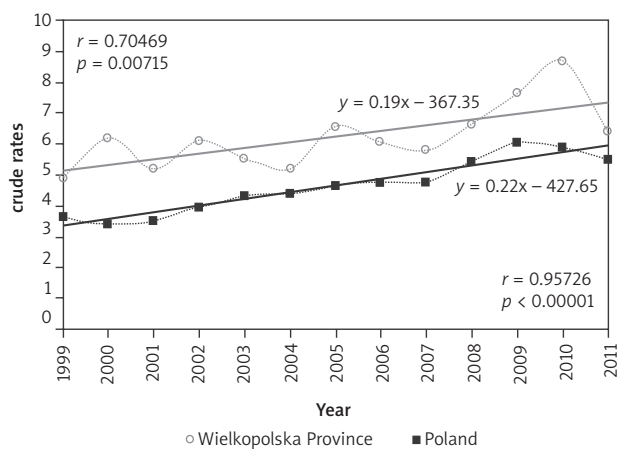


Fig. 1. Incidence trends among men with malignant testicular neoplasms in Poland and in Wielkopolska Province (crude rates) in the period of 1999–2011

Pearson’s correlation coefficient (R, the strength of linear correlation) differed significantly in the territory of Poland and Wielkopolska Province (crude rates: $p = 0.0295$, standardised rates: $p = 0.0337$). There was a stronger correlation, i.e. a more stable growth, observed in Poland than in Wielkopolska Province.

The multiple linear regression model used to thoroughly analyse the trends of malignant cancer incidence among men in Poland confirmed that the year is a strong incidence forecast factor ($p = 0.01998$). However, the independent impact of year on incidence rates in Wielkopolska was not revealed (Table 1).

The studied interaction between year and age also turned out to be important (approaching the level of statistical significance, $p = 0.09176$). This indicates that the increase in incidence is not steady in all age groups but pertains to young people to a greater extent (Table 2).

A corresponding age-group-specific analysis of mortality rates in the population of men in Poland and Wielkopolska Province did not reveal any statistically significant correlations (Figs. 3, 4).

The multiple linear regression model used in the thorough analysis of mortality rates among men due to malignant testicular neoplasms in Poland and in Wielkopolska Province indicated that the year variable is not an independent forecast factor (Table 3).

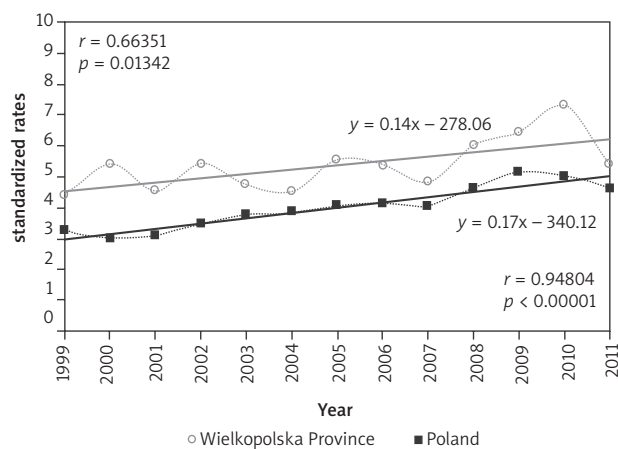


Fig. 2. Incidence trends among men with malignant testicular neoplasms in Poland and in Wielkopolska Province (standardized rates) in the period of 1999–2011

Table 1. Multiple regression model for the trends in malignant testicle tumour incidence among men in Poland and in Wielkopolska Province in the period 1999–2011

	Poland			Wielkopolska		
	b	stat. t	p-value	b	stat. t	p-value
Absolute term	-621.31	-2.32	0.02095	-514.28	-1.30	0.19516
Year	0.31	2.34	0.01998	0.26	1.32	0.18918
Age group	41.69	1.69	0.09262	38.00	1.04	0.29978
Year*age group	-0.02	-1.69	0.09176	-0.02	-1.05	0.29694

b – multiple regression equation coefficient
stat. t – Student-t statistics in the multiple linear regression model
p-value – Student-t test probability

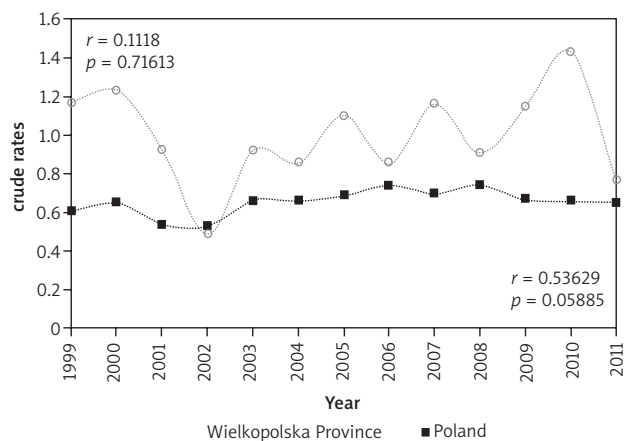


Fig. 3. Mortality rates among men due to malignant testicular neoplasms in Poland and in Wielkopolska Province (crude rates) in the period of 1999–2011

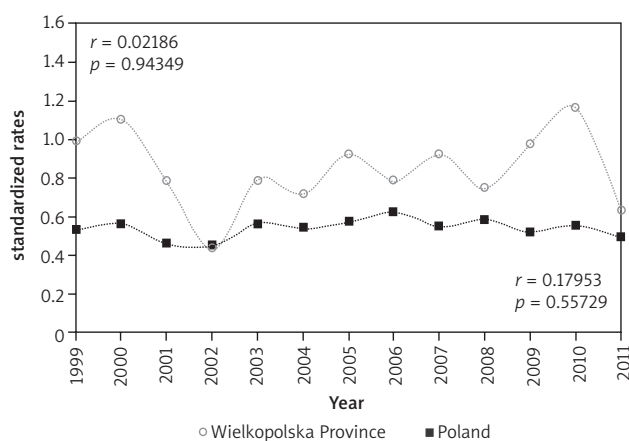


Fig. 4. Mortality rates among men due to malignant testicular neoplasms in Poland and in Wielkopolska Province (standardized rates) in the period of 1999–2011

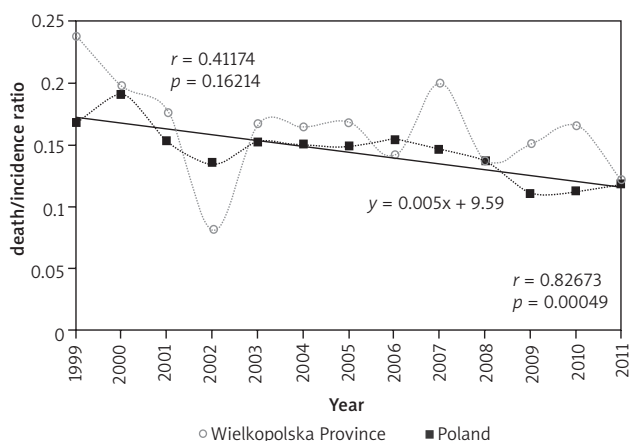


Fig. 5. The trend in death/incidence ratios in Poland and in Wielkopolska Province in the period of 1999–2011

Throughout the period subject to our study, a significantly decreasing tendency in the death/incidence ratio was observed only in the territory of Poland (Fig. 5).

Discussion

Geographical differences in the incidence due to testicular tumours had been observed for many years, the high-

Table 2. Analysis of age-group specific linear trend of malignant testicular neoplasms incidence among men in Poland and in Wielkopolska Province in the period 1999–2011

Age group	Poland		Wielkopolska	
	r	p-value*	r	p-value*
0–4 years	0.35849	0.22905	0.24662	0.41663
5–9 years	0.16968	0.57945	–	–
10–14 years	–0.03348	0.91353	–	–
15–19 years	0.73162	0.00448	0.08911	0.77222
20–24 years	0.82263	0.00055	0.03057	0.92102
25–29 years	0.94791	< 0.00001	0.63239	0.02038
30–34 years	0.93625	< 0.00001	0.34443	0.24914
35–39 years	0.88521	0.00006	0.17545	0.56643
40–44 years	0.68807	0.00933	0.28433	0.34644
45–49 years	0.70109	0.00759	0.45321	0.11987
50–54 years	0.63053	0.02087	0.23789	0.43383
55–59 years	0.07339	0.81169	–0.08616	0.77958
60–64 years	–0.06123	0.8425	0.3362	0.26137
65–69 years	–0.16457	0.59109	0.21939	0.47143
70–74 years	–0.52338	0.06643	–0.4943	0.08597
75–79 years	–0.7526	0.00299	–0.3061	0.30909
80–84 years	–0.52898	0.06306	–0.2909	0.33492
85+ years	–0.14252	0.64232	–0.1342	0.66204

r – Pearson's correlation coefficient

p-value* Pearson's correlation

The significance level for the p value in the table above has been modified according to Bonferroni adjustment and equals 0.0028

est incidence having been noted since 1940 in white men in the USA. For the subsequent 40–50 years the incidence was rising in western European countries [15].

In the 21st century the highest testicular tumour incidence has been observed in the countries of western and northern Europe as well as Australia and New Zealand, slightly lower incidence has been noted in North America, southern Europe, and Central America, and the lowest in Asia and Africa [3, 4, 7, 8, 16]. According to prediction, by 2025 1 in 100 men under 75 years of age will be diagnosed with this illness in Norway, Croatia, and Slovenia, the highest risk countries in Europe [17].

Malignant testicle tumour incidence among Polish men has increased by a factor of three in the past three decades (in 2011 there were almost 1100 noted cases) [11]. In the 2008 the incidence reached the level of 3.5/100,000 and was lower than the average level for EU countries (6.1/100,000) but higher than the average for Central and Eastern Europe (2.6/100,000 – data from 2008) [8, 11]. Out of 27 EU countries Poland was ranked eighth with respect to testicular cancer incidence rates among men, the lowest incidence rates having been observed in Greece, Romania, and Portugal, whereas the highest were noted in Denmark, Slovenia, and the Czech Republic [8].

Within the period subject to our study, the standardised testicular cancer incidence rates in men living in Wielkopolska were higher than the Polish average values, and in 2009 the incidence rate exceeded the average value for EU countries – 6.0/100,000 [11].

The described growing tendency in the testicular tumour incidence among men in Poland encompassed

Table 3. Multiple linear regression model for mortality rates among men due to malignant testicular neoplasms in Poland and in Wielkopolska Province in the period 1999–2011

	Poland			Wielkopolska		
	b	stat. t	p-value	b	stat. t	p-value
Absolute term	−44.68	−0.77	0.44482	−55.45	−0.30	0.76471
Year	0.02	0.76	0.44560	0.03	0.30	0.76472
Age group	6.39	1.18	0.23732	9.73	0.57	0.56993
Year *age group	0.00	−1.17	0.24451	0.00	−0.56	0.57525

b – multiple regression equation coefficient

stat. t – Student-t statistics in the multiple linear regression model

p-value – Student-t test probability

three increasing time trends observed in three age groups: among children (0–19 years), young adults (20–44 years), and middle-aged men (45–64 years), while in the group of 20–44-year-olds the incidence rate grew most rapidly [11].

In the period of 1999–2011, both the standardised and the crude malignant testicular cancer incidence rates indicated a significantly growing tendency in Poland and in Wielkopolska Province, which confirmed the specificity of testicular cancer incidence among men and its bimodal distribution [12]. The increasing trend in testicular tumour incidence observed in Poland was compliant with the time trends in many other countries [7, 8, 10, 17–19].

In the territory of Poland, an increasing incidence trend was observed in the four subsequent age groups, encompassing jointly men aged 20–39 years. In Wielkopolska Province, the growing incidence among young men has not shown any statistical significance.

The reasons for the growing malignant testicular cancer incidence that has been observed for the past 50 years all over the world, mostly in developed countries, as well as the differences in the course of its trends between various countries, remain unknown [7, 20]. The recognised risk factors, e.g. cryptorchidism, former testicular malignancy, intratubular germ cell neoplasia, family history of testicular cancer, being exposed to a high level of motherly oestrogens *in utero*, and fertility disorders, as well as better diagnostics and more precise statistics of incidence rates do not fully explain the diversity of trends [5, 8, 20].

More than 90% of testicular tumours stem from germ cells. There is no doubt that the ethnical background is one of the single, subordinate aetiological factors having an impact on the development of these tumours (the incidence is higher among white men living in industrialised countries, especially in northern Europe). The discrepancies observed all over the world, however, result from interactions between genetic factors and harmful impacts of the environment [3–5, 7, 8, 20].

The relationship between perinatal risk factor, congenital abnormalities, and the onset of the disease at a young age suggest that tumour formation may start in the womb, and its further development may be determined by such aspects as life style – diet, lack of physical activity, the type of work performed, or being exposed to harmful chemical substances [5, 7, 20]. Due to contradictory results of studies, the increase in the incidence among some men associated with the specificity of work they do and the exposure to such harmful factors as high

temperature in the scrotum, lack of physical activity due to extended sitting time, or the impact of electromagnetic fields require further detailed research [5, 7]. Just how little is known about testicular cancer risk factors can be seen from the results of research confirming an increase or a decline in risk of cancer caused by the same factors and sometimes negating their relationship with carcinogenesis. This refers to such aspects as body mass index (BMI), height, and physical activity [5, 7, 20]. Consumption of marijuana, exposure to high temperatures, and the potential impact of some viruses on the development of testicular tumours must also be confirmed in further epidemiological studies [7, 21].

Testicular cancer mortality rates, similarly to incidence rates, have revealed geographical diversity, characterised by the highest values observed in Central America, Central and Eastern Europe, and Western Asia and the lowest in Australia and Eastern Asia [16]. Starting from the 1970s, mortality rates have been decreasing significantly in most western and northern European countries, whereas the decline in mortality rates in central and eastern European countries started later (in the 1980s) and was considerably smaller. Also, the level of mortality in the countries of Southern Europe is higher than in the countries of western and northern Europe [22, 23].

Positive tendencies in mortality rates, associated with the improvements in diagnostics and chemotherapy efficiency (the inclusion of cisplatin into treatment regimens) that have been observed in most European countries in recent decades correspond to those reported in the USA [23, 24].

The mortality caused by testicular tumours in men increased in Poland until the beginning of the 1990s, after which there was a change in trends, with a significant decline. Nevertheless, the mortality rates are still slightly higher than the average rates in EU countries. The growing tendency was persistently the longest (until the beginning of the 21st century) among men aged 20–24 years [11]. In the period 1999–2011 there were no significant changes in mortality rates observed for the population of men in Poland and in Wielkopolska Province.

Testicular cancer is one of the most easily preventable malignancies, and early diagnosis and radical treatment increase the chance of survival of a significant proportion of patients [7, 14, 24]. Prognosis depends on the histological type of cancer, with the best being in the case of seminoma, which appear most often in men aged 35–40 years, and non-seminomatous tumours, occurring mostly among

25–29-year olds, whereas the forecast related to non-seminomatous germ cell tumours is the worst [7, 19, 25].

Summing up

Testicular tumour incidence rates in Poland are among the lowest in Europe and its growth corresponds to the tendencies evident in other countries. What is worrying is the fact that there has been a significant increase in incidence in the age group 20–39-year-olds as well as a lack of any significant declining trend in the mortality rate, which is slightly higher than the average for EU countries. A positive observation is the significant declining tendency in the death/incidence ratio. In the territory of Wielkopolska there has been an observed growing tendency of incidence, higher in comparison with the national average.

A high percentage of patients in Poland, whose tumours at the time of diagnosis are larger than 5 cm in diameter, or whose testicles are fully occupied by malignancy, indicate a long period of development of the disease prior to the diagnosis. Appropriate educational programs can contribute to earlier reporting of patients with a lower severity of the disease, thus increasing their chances of recovery [9]. Introducing preventive examinations in regions, such as Wielkopolska, characterised by increased risk of testicular tumour for boys and men aged 10–35, who for the previous five years have been treated for cryptorchidism, migrating, atrophic, hypotrophic testicles, Klinefelter syndrome, infertility, and testicular cancer, following the pattern of procedures adopted in Kraków, may allow earlier diagnosis [26]. In view of the fact that the increase of testicular tumour incidence in Poland begins among men from the age of 20, a thorough periodical check-up examinations of adolescents, including the assessment of sexual maturity, should be emphasised. The question is whether such examinations should be performed at school.

The authors declare no conflict of interest.

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