Intracranial Tumors in Adult Population of the Varaždin County (Croatia) 1996-2004: A Population-Based Retrospective Incidence Study

Biserka Dobec-Meić, MD, MS, Slaven Pikija, MD[1], Danijel Cvetko, MD[2], Vladimir Trkulja, MD, PhD[3], Leo Pažanin, MD, MS[4], Nenad Kudelić, MD[5], Krešimir Rotim, MD, PhD[6], Ruža Kostanjevec, MD, MS[1]

Department of Radiology, Jordanovac University Hospital for Pulmonary Diseases, Zagreb, Croatia
[1]Department of Neurology, Varaždin General Hospital, Varaždin, Croatia
[2]Department of Radiology, Varaždin General Hospital, Varaždin, Croatia
[3]Department of Pharmacology, School of Medicine, University of Zagreb, Zagreb, Croatia
[4]Department of Neuropathology, Zagreb University Hospital Center, Zagreb, Croatia
[5]University Department of Neurosurgery, Sestre milosrdnice University Hospital, Zagreb, Croatia
[6]University Department of Neurosurgery, Dubrava University Hospital, Zagreb, Croatia

Corresponding author:
Slaven Pikija
Djelatnost za neurologiju
Opća bolnica Varaždin
I. Meštrovića bb
HR-42000 Varaždin
Croatia

Phone: +385 42 393329 Mobile: +38598379788 E-mail: pikija.slaven@vz.t-com.hr

Running title: Intracranial tumors in Varaždin, Croatia

ABSTRACT

AIM: To estimate the incidence of intracranial tumors in the adult population of the Varaždin County, Croatia, for the 1996-2004 period.

METHODS: Setting: Varaždin County General Hospital and four university hospitals in Zagreb, the capital of Croatia. Study period: January 1,1996 to December 31, 2004. Incident patients: county residents admitted for newly diagnosed intracranial tumors according to the WHO diagnostic criteria. Demographic data were extracted from the 2001 Croatian census. Incidence rates (IR) *per* 100000 person-years (p-y) and annual IRs (*per* 100000 persons) were determined and compared as incidence rate ratios (IRR) with 95% CI.

RESULTS: For primary intracranial tumors (PIT), IR was 12.1/100000 p-y (95% CI 10.3 to 14.2), comparable in men and women. The highest incidence was recorded for glioblastoma (IR 4.8, 3.7 to 6.2) and meningioma (IR 3.1, 2.2 to 4.2). The incidence of PIT was somewhat greater than that of metastatic tumors (IRR 1.58, 95% CI 1.22 to 2.05, $p<0.001$). Metastatic tumors were more frequent in men than in women, especially metastatic lung tumors (IRR 6.08, 2.32 to 20.16, $p<0.001$). IRs of all PIT taken together, neuroepithelial tumors cumulatively, non-epithelial tumors cumulatively, glioblastoma and meningioma were higher in the population aged ≥40 *vs.* population aged ≤39 (all IRRs with 95% CI greater than 1, $p<0.05$ or <0.001), comparable in men and women. Women were somewhat older than men at the time of diagnosis of PIT: median difference -6 years (95.1% CI -10 to -1, $p<0.05$). Annual IRs for all these tumor categories showed increasing trends over the study period.

CONCLUSION: Overall, there was an increasing trend in the incidence of primary intracranial tumors in the Varaždin County. Data did not allow estimation for most of the specific tumor types.

Key words: Intracranial tumors; Croatia; epidemiology

Introduction

Intracranial tumors bear unfavorable clinical prognosis merely by their localization. Primary intracranial tumors arise from intracranial cell mutagenesis, triggers of which are largely unknown. The most common primary intracranial tumors in adults are those of neuroepithelial origin. Regarding specific tumor types, the most frequent are gliomas, followed by meningiomas and pituitary gland tumors [1-4]. Men appear to be at an increased risk of developing gliomas as compared to women, whereas the risk of developing meningioma appears to be lower in men [1]. Secondary or metastatic intracranial tumors may originate from different sites. Of "peripheral" tumors, lung cancer (*carcinoma bronchii*) is the most likely one to spread intracranially, followed by breast carcinoma [9]. Metastatic intracranial tumors are more frequent in men than in women due to the higher incidence of lung cancer in men [9].

Epidemiological studies have indicated a steady increase in incidence rates of intracranial tumors over the last few decades in both sexes and in all age groups [3,6-9], although there has been some debate about whether the increasing trends are true or artifactual [10]. Unlike many other countries [4,7,11,12,13,14,15], epidemiological data on intracranial tumors in the adult population in Croatia have been rather incomplete since the early 1990s – there are some regional reports [16], and the existing Croatian Cancer Registry [17] is not consistently updated [16]. We aimed to assess regional epidemiological data on intracranial tumors in the adult population of the Varaždin County. We believe this would help in establishing the grounds for future observational studies that would, eventually, contribute to regaining a proper insight into the epidemiology of intracranial tumors at the national level.

Subjects and Methods

Study design

This was a retrospective population-based incidence study. Incident patients ("cases") were defined as adult (≥18 years of age) Varaždin County residents with newly diagnosed intracranial tumors according to the WHO diganostic criteria [1] during the period between January 1, 1996 and December 31, 2004. All "cases" were embraced with MRI or CT imaging. Demographic data on the Varaždin County population were extracted from the Croatian 2001 census [18].

Varaždin County population

Varaždin County is located in the outermost northwestern part of Croatia. With 1261.29 km² it is one of the smallest Croatian counties. According to the 2001 census, the Varaždin County population was 184769, 84839 (48.6%) men and 94930 (51.4%) women, accounting for 4.2% of the total Croatian population. The Varaždin County adult population (≥18 years of age) was 144634, 69488 (48.0%) men and 75498 (52.0%) women. The population density of 146.6 inhabitants/km² makes it one of the most populous counties in Croatia. The population is located in 6 towns (the largest one and the County capital is Varaždin) and 22 communities. Approximately 55% of the inhabitants live in urban and 45% in rural parts of the County. The total number of inhabitants increased by only about 5000 over a 30-year period (1971-2001), indicating a stability in demographic variation [18].

Varaždin County economy and healthcare system

The economy is based on textile and food industry, agriculture, hunt and forestry, architecture and building and distribution companies. The healthcare system consists of 101 primary healthcare teams organized through 4 medical centers (Varaždin, Ludbreg, Ivanec and Novi Marof), County Public Health Institute, Varaždin County General Hospital, 3 special hospitals (Klenovnik, Novi Marof and Varaždinske Toplice), and several private institutions. During the

study period, there were two CT units and no MRI units in the Varaždin County. The Varaždin County inhabitants commonly seek medical services in the capital (Zagreb) due to its proximity.

Data collection

Varaždin County General Hospital is the only medical institution in the County equipped for the diagnosis and treatment of malignant diseases. However, not to miss potential "cases" that have not been, at any instance, admitted to the County hospital, we searched not only the central database at the hospital but also databases at the main institutions in Zagreb that deal with intracranical tumors and malignant diseases in general: Zagreb University Hospital Center, Sestre milosrdnice University Hospital, Jordanovac University Hospital for Pulmonary Diseases, and Dubrava University Hospital. Every effort was made to obtain all valuable information. Incident patients were identified, assigned identification codes, and data on their demographics, date and age of the tumor diagnosis and tumor type (pathohistologic diagnosis) were retrieved.

For primary intracranial tumors (n=158), pathohistologic confirmation was established in 133 (84%) patients, a rate comparable to "pathohistologic confirmation" rates reported from other studies in different countries, e.g., Switzerland (75% to 95%), Canada (27% to 91%), Brazil (45% to 87%) and United States (63% to 99%) [19]. The pathohistologic confirmation for presumed secondary intracranial masses was around 45%. For secondary tumors without a pathohistologic diagnosis we reviewed neuroradiologic reports (available in all cases). When the images showed multiple intracranial tumors remote from the dura that were accompanied by clinical information on a systemic malignant disease, we considered the lesions as metastatic tumors [13].

Determination of incidence rates

Considering the reported stability of the total number of inhabitants in the Varaždin County between 1971 and 2001, we used the 2001 census data as a basis for calculation of incidence rates [18]. Since the study was focused on adult patients, i.e., patients aged ≥18, the demographic

basis was 144634 inhabitants, 69488 men and 75498 women [18]. All incidence rates referring to the entire study period (1996-2004) were determined *per* 100000 person-years (p-y). Annual incidence rates were determined *per* 100000 inhabitants.

Data handling and statistical analysis

Database was built using Microsoft Access version 2000 (Microsoft Inc., Seattle, WA, USA). Summary statistics is reported on sex and age at diagnosis for the incident patients. Difference in the age at diagnosis between men and women was determined as a median difference with 95.1% approximate confidence intervals (CI), and statistical significance was tested using the Mann-Whitney U-test. Incidence rates (IR) and all other epidemiologic indices are reported with the Poisson-based 95% CI. Difference between two incidence rates is given as an incidence rate ratio (IRR) employing the conditional maximum likelihood estimation and exact confidence intervals. Annual incidence rate curves were shown as "true" IRs and smoothed curves, using the "rolling average" approach. Rolling four-year medians of incident patients were calculated and expressed as IR *per* 100000 persons (four-year rolling average IR). We used StatsDirect version 2.3.8 software (StatsDirect Ltd., Cheshire, UK, 2004).

Results

Total and sex- and age-specific incidence according to tumor type

For the period between January 1, 1996 and December 31, 2004, we identified a total of 264 Varaždin County residents aged ≥18 with newly diagnosed intracranial tumors (incident patients), yielding an incidence rate of 20.3/100000 p-y. Table 1 presents the number of incident patients according to tumor type and sex, and Table 2 shows corresponding incidence rates and menwomen incidence rate ratios. There were more incident men than women, yielding an IR greater by 38% in men (95% CI for IRR 1.08 to 1.78; p=0.01) (Table 2). The incidence rate of primary intracranial tumors (158 cases, IR=12.1/100000 p-y) was higher than the incidence rate of metastatic tumors (99 cases, IR=7.6/100000 p-y); IRR=1.58, 95% CI 1.22 to 2.05, p<0.001. The incidence of metastatic intracranial tumors was by 152% higher in men than in women (p<0.001): by 508% higher in case of metastatic lung tumors (p<0.001) and by 90% higher for tumors of other origin (p=0.013) (Table 2). According to the origin, primary intracranial tumors were more frequently neuroepithelial (87 cases, IR=6.7/100000 p-y) than nonepithelial (71 cases, IR=5.5/100000 p-y) (Tables 1 and 2) – IRR=1.23 (95% CI 0.89 to 1.70). There appeared to be no major sex difference in the incidence of primary intracranial tumors, either neuroepithelial or nonepithelial (Table 2). According to histologic type, glioblastoma showed highest incidence among primary intracranial tumors (63 cases, IR=4.8/100000 p-y), which was comparable in men and women (Tables 1 and 2), followed by meningioma (40 cases, IR 3.1/100000 p-y) which, however, showed a higher incidence (by 28%) in women than in men (Tables 1 and 2). Other tumor types with IRs >0.2/100000 p-y were pituitary adenoma (IR=0.8), schwannoma (IR=0.6), anaplastic astrocytoma (IR=0.5), and astrocytoma, ependymoma, primary malignant lymphoma and anaplastic oligodendroglioma, IR 0.3 each (Tables 1 and 2).

Except for glioblastoma and meningioma, the incidence of specific primary intracranial tumor types was too low for evaluation of age-specific incidence rates. The overall incidence rate of

primary intracranial tumors, of neuroepithelial tumors cumulatively, of nonepithelial tumors cumulatively, and of glioblastoma and meningioma all showed a similar rising pattern in older age groups, peaking in the 60-69 or 70-79 age groups (Figure 1). For all these "tumor categories" IRs were clearly higher in the population aged ≥40 as compared with the population aged ≤39 (Figure 2). In both age groups, IRs of all "tumor categories" were comparable between men and women, although there was a trend of higher IR of neuroepithelial tumors in men *vs.* women in the ≤39 age group (IRR 4.21, 95% CI 0.89 to 40.07), and a trend of lower IR of nonepithelial tumors in men *vs.* women in the ≥40 age group (IRR 0.76, 95% CI 0.44 to 1.30) (Figure 2). Generally, women were somewhat older than men at the time of diagnosis for all main "tumor categories" (Table 3).

Annual incidence of primary intracranial tumors – total and sex-specific

When all primary intracranial tumors were considered cumulatively, annual IRs (*per* 100000 population) were rather variable between 1996 and 2004 (Figure 3). However, smoothed (rolling average) curves indicated an increasing trend from 1999 towards 2004, for both men and women (Figure 3). A very similar pattern was observed for neuroepithelial tumors cumulatively (increasing trend somewhat more prominent in men) and for nonepithelial tumors cumulatively (increasing trend somewhat more prominent in women) (Figure 3). There appeared to be no obvious trend in the incidence of glioblastoma or meningioma (Figure 3).

Discussion

Epidemiologic data on intracranial tumors in the adult Croatian population have been rather incomplete since the early 1990s [16]. The present study attempted to estimate the incidence of intracranial tumors in the adult population in one of the Croatian counties (Varaždin County) for the period between 1996 and 2004. The obvious limitation of the study was its retrospective design and the fact that it was based on hospital database searches. Consequently, it is possible that the results were confounded by underreporting, i.e., missed "cases". However, we believe that the reported rates are fairly accurate since the search for incident patients included all relevant institutions to which the County population are referred, i.e. Varaždin County General Hospital, which is the only institution in the County equipped for the diagnosis and treatment of malignant diseases, and four university hospitals in the nearby state capital Zagreb. The fact that the observed incidence rate of primary intracranial tumors (12.1/100000 person-years) was comparable to that reported for the whole Croatia in 1991 (11.7/100000 person-years) [17], when the central Croatian Registry was still functioning, supports the validity of the current observations. Also, this incidence rate does not appear to differ much from that reported from the United States Central Brain Tumor Registry for the similar time period (1997-2001) (14.1/100000 person-years) [12]. As expected [1-4], glioblastoma was a primary intracranial tumor of the highest incidence, followed by meningioma and pituitary adenoma. However, except for glioblastoma and meningioma, the incidence rates of particular tumor types were very low. Therefore, the analysis was restricted to a few "tumor categories", i.e. primary intracranial tumors overall, neuroepithelial tumors cumulatively, nonepithelial tumors cumulatively, glioblastoma and meningioma. Several of the present observations regarding primary intracranial tumors are in agreement with those reported by others: there was an increasing trend in the overall incidence of primary intracranial tumors, both neuroepithelial and nonepithelial (although this was not obvious for glioblastoma or meningioma) [3,6-9]. The incidence rates of all "tumor

categories" analyzed tended to increase with age [4,12,20], and the incidence rate of meningioma tended to be greater in women than in men [3,5,12]. On the other hand, the incidence rates of neuroepithelial tumors (cumulatively) appeared to be comparable for men and women, whereas a higher incidence in men has been reported elsewhere [3,5,12]. Also, women appeared to be at an older age at the time of diagnosis than men, whereas some studies report opposite findings [13]. Overall, however, the present data do not seem to deviate much from other respective literature reports.

In the present study, the incidence rate of metastatic tumors appeared to be somewhat lower than that reported for Croatia in 1991 [17] (7.6 *vs.* 9.4/100000 person-years). This discrepancy might have been due to underreporting of metastatic intracranial tumors, which is a common phenomenon and might be due to a variety of reasons [21]. The incidence rate of metastatic tumors was clearly much higher in men than in women. This was most likely due to a great difference in the incidence of lung carcinoma between Croatian men and women, a phenomenon related to the higher prevalence of smokers among men [17].

In conclusion, we conducted a retrospective incidence study to assess the regional epidemiologic data on intracranial tumors in the adult population in one of the Croatian counties (Varaždin County) for the 1996-2004 period. Considering primary intracranial tumors, the present data do not seem to deviate much from the similar literature reports. Since the epidemiologic data on intracranial tumors in Croatia have been rather incomplete, we believe that this effort would help in establishing the grounds for future observational studies that would, eventually, contribute to regaining a proper insight into the epidemiology of intracranial tumors at the national level.

References

1 Kleihues P, Burger PC, Scheithauer BW: The new WHO classification of brain tumours. Brain Pathol 3: 255-68, 1996

2 Kaye SH, Laws ER Jr: Gliomas, in Kaye AH, Laws ER Jr (eds): Brain Tumors. Edinburgh, Churchill Livingstone, 1995, pp 433-560

3 D'Alessandro G, Di Giovanni M, Ianizzi L, Guidetti E, Bottachi E: Neuroepidemiology of primary intracranial tumors in the Valle d'Aosta (Italy) during the 6-year period 1986-1991. Neuroepidemiology 14: 139-46, 1995

4 Christensen HC, Kosteljanetz M, Johansen C: Incidence of gliomas and meningiomas in Denmark, 1943 to 1997. Neurosurgery 52: 1327-1334, 2003

5 Fogelholm R, Uutela T, Murros K: Epidemiology of central nervous system neoplasms. A regional survey in Central Finland. J Neurosurg 83: 999-1003, 1995

6 Posner JB, Chernik NL: Intracranial metastases from systemic cancer. Adv Neurol 19: 579-592, 1978

7 Mao Y, Desmeules M, Semenciw RM, Hill G, Gaudette L, Wigle DT: Increasing brain cancer rates in Canada. Can Med Assoc J 145: 1583-1591, 1991

8 Helseth A: Increasing incidence of primary central nervous system tumors in the elderly: real increase or improved detection? J Natl Cancer Inst 85:1871-1872, 1993

9 Counsell CE, Collie DA, Grant R: Incidence of intracranial tumours in the Lothian region of Scotland, 1989-1990. J Neurol Neurosurg Psychiatry 61: 143-150, 1996

10 Gurney JG, Kadan-Lottick N: Brain and other central nervous system tumors: rates, trends and epidemiology. Curr Opin Oncol 13: 160-166, 2001

11 Shugg D, Allen BJ, Blizzard L, Dwyer T, Roder D: Brain cancer incidence, mortality and case survival from two Australian cancer registries. Int J Cancer 59: 765-770, 1994

12 CBTRUS (2004). Statistical report: Primary brain tumors in the United States Statistical Report 1997-2001. Published by the Central Brain Tumor Registry of the United States.

13 Pobereskin LH, Chadduck JB: Incidence of brain tumours in two English counties: a population based study. J Neurol Neurosurg Psychiatry 69: 464-471, 2000

14 Shibamoto Y, Tsuchida E, Seki K, Oya N, Hasegawa M, Toda Y, Takemoto M, Sumi M, Hiratsuka J, Oguchi M, Hosono M, Yasuda S, Sougawa M, Kakutoh Y, Hayabuchi N: Primary central nervous system lymphoma in Japan 1995-1999: changes from the preceding 10 years. J Cancer Res Clin Oncol 130(6): 351-6, 2004

15 van der Sanden GA, Schouten LJ, van Dijck JA, van Andel JP, van der Maazen RW, Coebergh JW; Working Group of Specialists in Neuro-Oncology in the Southern and Eastern Netherlands: Primary central nervous system lymphomas: incidence and survival in the Southern and Eastern Netherlands. Cancer 94(5): 1548-56, 2002

16 Materljan E, Materljan B, Sepčič J, Tuškan-Mohar L, Zamolo G, Erman-Baldini I: Epidemiology of central nervous system tumors in Labin area, Croatia,1974-2001. Croatian Med J 45(2): 206-212, 2004

17 Cancer incidence in Croatia. Bulletins No. 13-23. Zagreb: Croatian National Institute of Public Health; 1993-2001

18 Census of population, households and dwellings, March 31, 2001. Population by sex and age, by settlements. Available at: http://www.dzs.hr. Accessed: February 1, 2005

19 Preston-Martin S: Epidemiology of primary CNS neoplasms. Neurol Clin 14:273-290, 1996

20 Parkin DM, Muir CS: Cancer incidence in five continents. IARC Sci Publ 120: 45-173, 1992

21 Klos KJ, O'Neill BP; Brain metastases. Neurologist 10(1): 31-46, 2004

Table 1. Number of patients with intracranial tumors in the Varaždin County population aged ≥18 (total 144634, 69488 men, 75409 women, see Patients and Methods) for the 1996-2000 period

Tumor type	Men	Women	Total (%)*
Primary intracranial	73	85	158 (100.0)*
Neuroepithelial	44	43	87 (55.1)
Other primary	29	42	71 (44.9)
By histology			
Glioblastoma	32	31	63 (39.9)
Meningioma	16	24	40 (25.3)
Pituitary adenoma	7	4	11 (7.0)
Schwannoma	2	6	8 (5.1)
Anaplastic astrocytoma	4	3	7 (4.4)
Astrocytoma	2	2	4 (2.5)
Ependymoma	2	2	4 (2.5)
Primary malignant lymphoma	1	3	4 (2.5)
Anaplastic oligodendroglioma	3	1	4 (2.5)
Oligodendroglioma	0	3	3 (1.9)
Craniopharyngioma	1	2	3 (1.9)
Anaplastic oligoastrocytoma	1	1	2 (1.3)
Anaplastic ganglioglioma	1	0	1 (0.6)
Medulloblastoma	1	0	1 (0.6)
Hemangioblastoma	0	1	1 (0.6)

Anaplastic meningioma	1	0	1 (0.6)
Pineal parenchymal tumors	0	1	1 (0.6)
Metastatic	70	29	99 (100.0)*
Lung tumors	28	5	33 (33.3)
Other primary sites	42	24	66 (66.6)
Cysts and tumor-like lesions	1	2	3*
Unknown	4	0	4*
Total	148	116	264

*Percentage used different denominators: for primary tumors, the total number of these tumors was considered as 100% and a breakdown by neuroepithelial origin (yes or no) and further histologic type is given. For metastatic tumors, the total number of such tumors was considered as 100%. Cysts and tumor-like lesions are not given in percentage. They represented around 1% of the total number of the lesions counted each.

Table 2. Incidence rates (IR) *per* 100000 person-years and men/women rate ratios (IRR) (with 95% CI) determined from data in Table 1 (only for tumors with at least 2 recorded "cases")

Tumor type	Total IR (95% CI)	Men IR	Women IR	Men/women IRR (95% CI)	P-value
Primary intracranial	12.1 (10.3 to 14.2)	11.7	12.5	0.93 (0.67 to 1.29)	0.691
Neuroepithelial	6.7 (5.4 to 8.2)	7.0	6.3	1.11 (0.71 to 1.73)	0.668
Non-epithelial	5.5 (4.3 to 6.9)	4.6	6.2	0.75 (0.45 to 1.23)	0.238
By histology					
Glioblastoma	4.8 (3.7 to 6.2)	5.1	4.6	1.12 (0.66 to 1.89)	0.706
Meningioma	3.1 (2.2 to 4.2)	2.6	3.5	0.72 (0.36 to 1.42)	0.345
Pituitary adenoma	0.8 (0.4 to 1.5)	1.1	0.6	1.9 (0.48 to 8.84)	0.372
Schwannoma	0.6 (0.3 to 1.2)	0.3	0.9	0.36 (0.04 to 2.02)	0.292
Anaplastic astrocytoma	0.5 (0.2 to 1.1)	0.6	0.4	1.45 (0.24 to 9.88)	0.717
Astrocytoma	0.3 (0.08 to 0.8)	0.3	0.3	1.09 (0.08 to 14.97)	0.999
Ependymoma	0.3 (0.08 to 0.8)	0.3	0.3	1.09 (0.08 to 14.97)	0.999
Primary malignant lymphoma	0.3 (0.08 to 0.8)	0.2	0.4	0.36 (0.007 to 4.5)	0.626
Anaplastic oligodendroglioma	0.3 (0.08 to 0.8)	0.5	0.1	3.26 (0.26 to 170)	0.356
Oligodendroglioma	0.2 (0.05 to 0.7)	0	0.4	0 (0 to 2.26)	0.251
Craniopharyngioma	0.2 (0.05 to 0.7)	0.2	0.3	0.52 (0.009 to 10.42)	0.999
Anaplastic oligoastrocytoma	0.2 (0.02 to 0.6)	0.2	0.1	1.09 (0.01 to 85.19)	0.999
Metastatic	7.6 (6.2 to 9.3)	11.2	4.3	2.62 (1.68 to 4.19)	< 0.001
Lung tumors	2.5 (1.7 to 3.6)	4.5	0.7	6.08 (2.32 to 20.16)	< 0.001

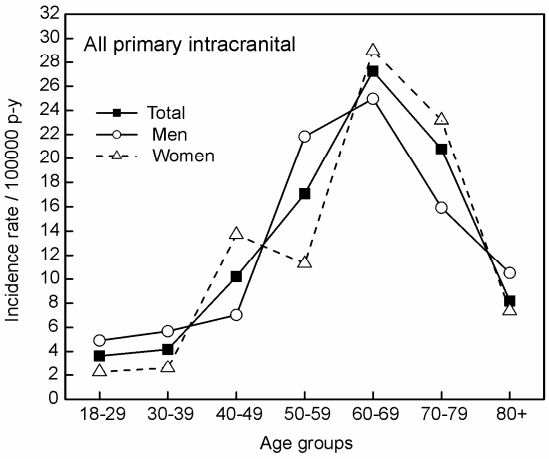
Other primary sites	5.1 (3.9 to 6.5)	6.7	3.5	1.90 (1.12 to 3.18)	0.013
Cysts and tumor-like lesions	0.2 (0.05 to 0.7)	0.2	0.3	0.52 (0.009 to 10.42)	0.999
Unknown	0.3 (0.08 to 0.8)	0.6	0	infinity	
Total	20.3 (17.9 to 22.9)	23.7	17.1	1.38 (1.08 to 1.78)	0.01

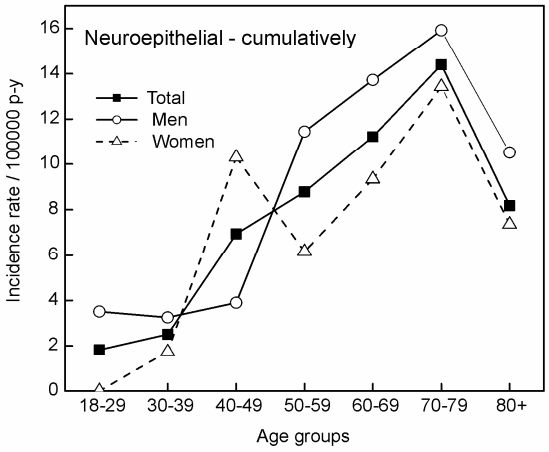
Table 3. Patient age (years) at diagnosis of intracranial tumors (by type) in the Varaždin County for the 1996-2004 period. Data are medians (quartiles). Median difference between men and women with 95.1% CI is given for the main tumor groups

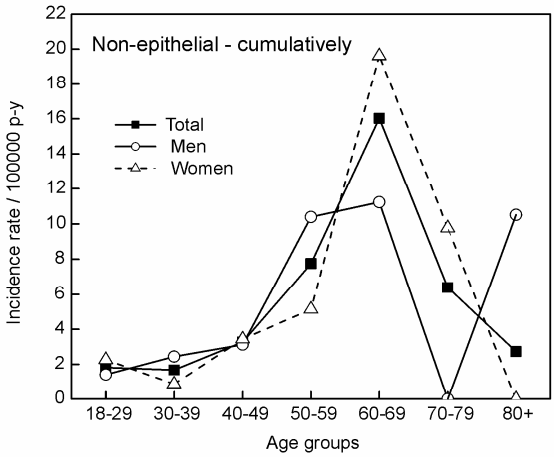
	Age at diagnosis			Men-women
	Men	Women	Total	
Primary intracranial	56 (46-65)	63 (49-69)	60 (48-68)	-6 (-10 to -1)*
Neuroepithelial	55.5 (43-66.5)	61 (48-71)	58 (47-69)	-5 (-12 to 2)
Nonepithelial	56 (48-61)	63 (55-67)	61 (50-67)	-7 (-12 to -1)*
By histology				
Glioblastoma	61.5 (52-68.5)	66 (49-72)	63 (50-71)	-4 (-10 to 4)
Meningioma	56.5 (48.5-63)	65 (61-69)	61 (55-67)	-9 (-15 to -1)*
Pituitary adenoma	55 (31-57)	59 (35.5-69.8)	55 (31-61)	
Schwannoma	64 (59-69)	65 (59.3-68.5)	65 (59.5-68-8)	
Anaplastic astrocytoma	49 (44-51)	66 (51-81)	51 (47-66)	
Astrocytoma	27 (24-30)	45.5 (43-48)	36.5 (25.5-46.8)	
Ependymoma	42 (28-56)	51 (48-54)	51 (33-55.5)	
Primary malignant lymphoma	66	62 (60-66)	64 (60.5-66)	
Anaplastic oligodendroglioma	68 (32-73)	36	52 (33-71.5)	
Oligodendroglioma	---	61 (48-68)	61 (48-68)	
Craniopharyngioma	68	24.5 (22-27)	27 (22-68)	
Anaplastic oligoastrocytoma	26	43	34.5 (26-43)	
Anaplastic ganglioglioma	33	---	33	

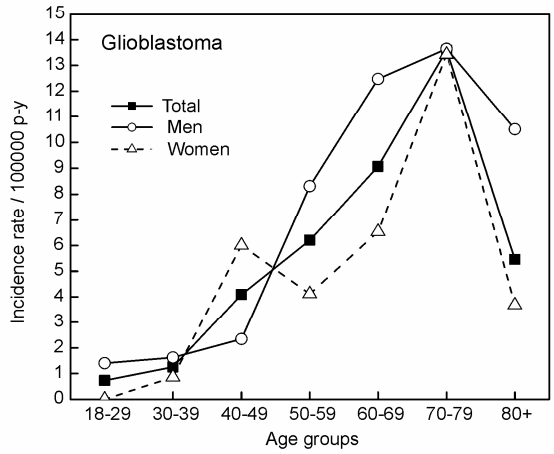
Medulloblastoma	23	---	23	
Hemangioblastoma	27	---	27	
Anaplastic meningioma	---	55	55	
Pineal parenchymal tumors	---	44	44	
Metastatic	63 (57-69)	68 (59-70)	64 (57-69.5)	-2 (-6 to 2)
Lung tumors	63.5 (58-70.5)	70 (68-73)	64 (58-71)	-6 (-16 to 3)
Other primary sites	62.5 (55-68)	66.5 (55.5-69)	63.5 (55-69)	-1.5 (-6 to 4)
Cysts and tumor-like lesions	29	30 (25-35)	44	
Unknown	47.5 (36-58.3)	---	47.5 (36-58.3)	
Total	60 (50-68)	63 (50.5-69.8)	61 (50-69)	-3 (-6 to 0)**

*p<0.05; **p=0.086; (Mann-Whitney U-test)


All primary intracranital
Total
Men
Women
Incidence rate / 100000 p-y
Age groups
18-29
30-39
40-49
50-59
60-69
70-79
80+


Neuroepithelial - cumulatively
Total
Men
Women
Incidence rate / 100000 p-y
Age groups
18-29
30-39
40-49
50-59
60-69
70-79
80+


Non-epithelial - cumulatively
Total
Men
Women
Incidence rate / 100000 p-y
Age groups
18-29
30-39
40-49
50-59
60-69
70-79
80+


Glioblastoma
Total
Men
Women
Incidence rate / 100000 p-y
Age groups
18-29
30-39
40-49
50-59
60-69
70-79
80+

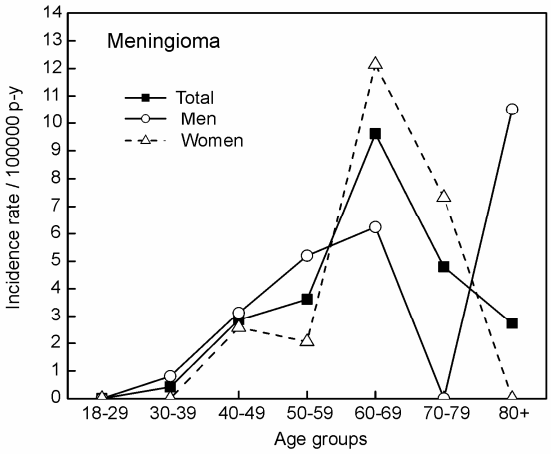
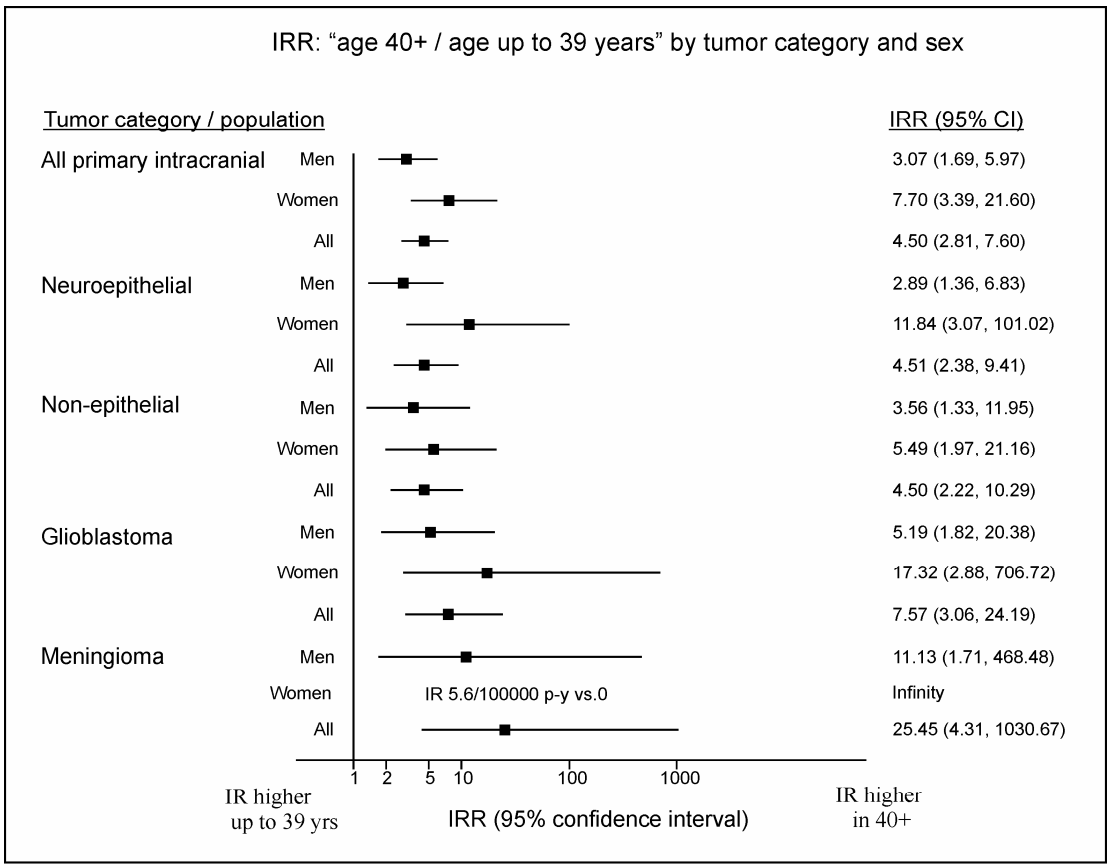

Meningioma
Total
Men
Women
Incidence rate / 100000 p-y
Age groups
18-29
30-39
40-49
50-59
60-69
70-79
80+

Figure 1. Age-specific incidence rates (*per* 100000 person years) of primary intracranial tumors in the adult population (≥18 years of age) of the Varaždin County for the 1996-2004 period, overall and by sex. Except for glioblastoma and meningioma, data for specific tumor types are not shown due to low incidence.


IRR: “age 40+ / age up to 39 years” by tumor category and sex
Tumor category / population
IRR (95% CI)
All primary intracranial
Men
3.07 (1.69, 5.97)
Women
7.70 (3.39, 21.60)
All
4.50 (2.81, 7.60)
Neuroepithelial
Men
2.89 (1.36, 6.83)
Women
11.84 (3.07, 101.02)
All
4.51 (2.38, 9.41)
Non-epithelial
Men
3.56 (1.33, 11.95)
Women
5.49 (1.97, 21.16)
All
4.50 (2.22, 10.29)
Glioblastoma
Men
5.19 (1.82, 20.38)
Women
17.32 (2.88, 706.72)
All
7.57 (3.06, 24.19)
Meningioma
Men
11.13 (1.71, 468.48)
Women
IR 5.6/100000 p-y vs.0
Infinity
All
25.45 (4.31, 1030.67)
1 2 5 10 100 1000
IR higher up to 39 yrs
IRR (95% confidence interval)
IR higher in 40+

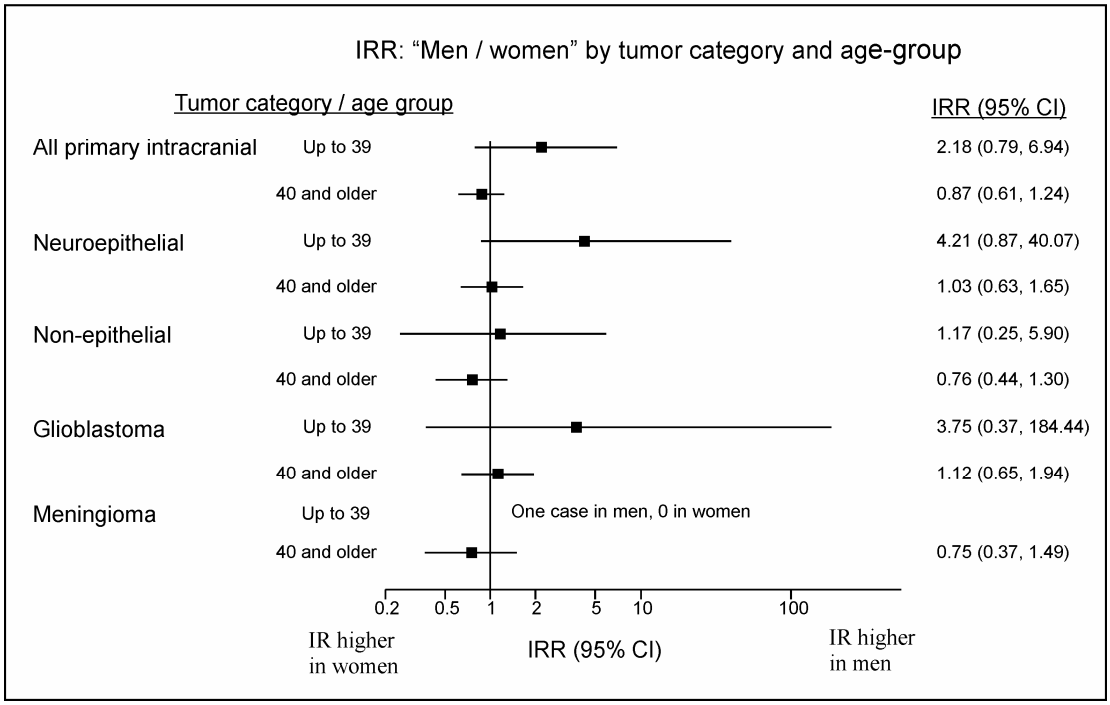
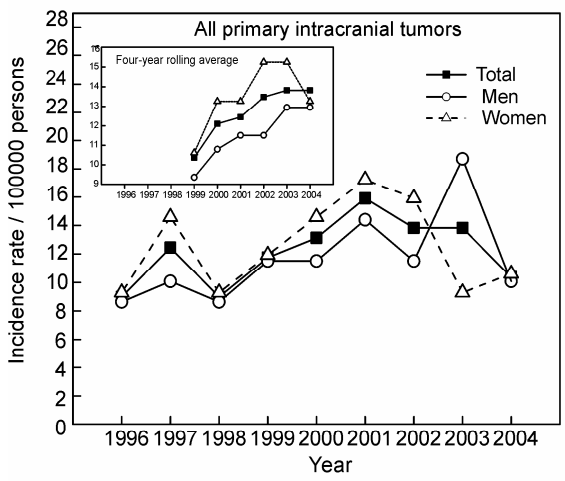
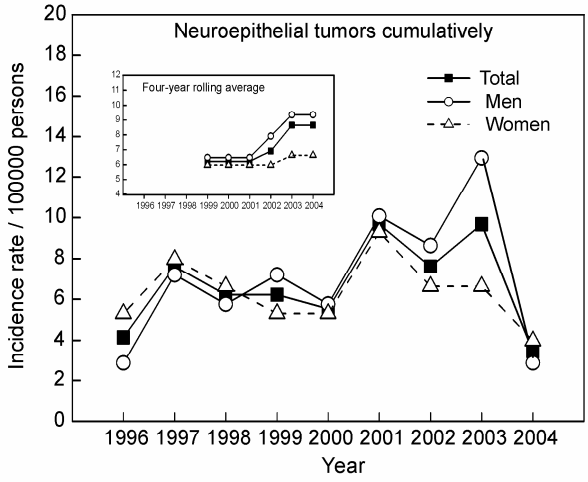
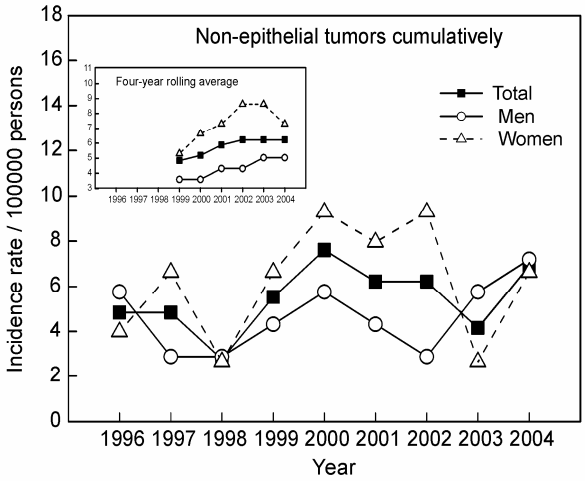
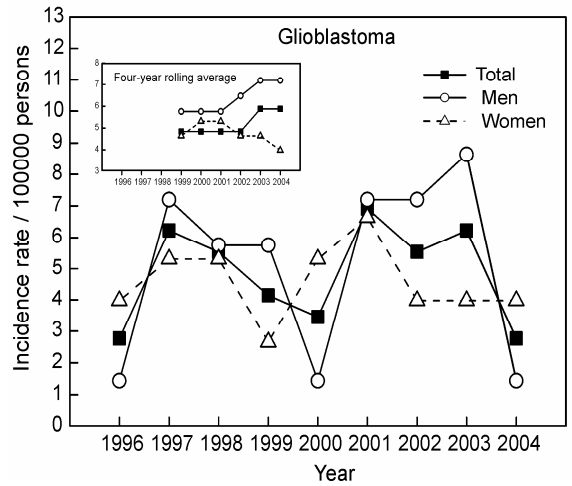

IRR: “Men / women” by tumor category and age-group
Tumor category / age group
IRR (95% CI)
All primary intracranial
Up to 39
2.18 (0.79, 6.94)
40 and older
0.87 (0.61, 1.24)
Neuroepithelial
Up to 39
4.21 (0.87, 40.07)
40 and older
1.03 (0.63, 1.65)
Non-epithelial
Up to 39
1.17 (0.25, 5.90)
40 and older
0.76 (0.44, 1.30)
Glioblastoma
Up to 39
3.75 (0.37, 184.44)
40 and older
1.12 (0.65, 1.94)
Meningioma
Up to 39
One case in men, 0 in women
40 and older
0.75 (0.37, 1.49)
0.2 0.5 1 2 5 10 100
IR higher in women
IRR (95% CI)
IR higher in men

Figure 2. Differences in incidence rates of primary intracranial tumors according to age and sex, by "tumor category" (all primary, neuroepithelial cumulatively, nonepithelial cumulatively, glioblastoma, meningioma). **Upper panel:** incidence rate ratios (IRRs, 95% CI) for the population aged ≥40 (40+) *vs.* population aged ≤39, according to sex. IRR above 1 indicates higher IR in older population, and IR below 1 indicates higher IR in younger population. For all IRRs *p* values were <0.05 or <0.001. **Lower panel:** men/women IRRs according to age groups (≥39 or ≥40). IRR above 1 indicates higher IR in men, and IRR below 1 indicates higher IR in women.


All primary intracranial tumors
Four-year rolling average
Total
Men
Women
Incidence rate / 100000 persons
Year
1996 1997 1998 1999 2000 2001 2002 2003 2004


Neuroepithelial tumors cumulatively
Four-year rolling average
Total
Men
Women
Incidence rate / 100000 persons
Year
1996 1997 1998 1999 2000 2001 2002 2003 2004


Non-epithelial tumors cumulatively
Four-year rolling average
Total
Men
Women
Incidence rate / 100000 persons
Year
1996 1997 1998 1999 2000 2001 2002 2003 2004


Glioblastoma
Four-year rolling average
Total
Men
Women
Incidence rate / 100000 persons
Year
1996 1997 1998 1999 2000 2001 2002 2003 2004

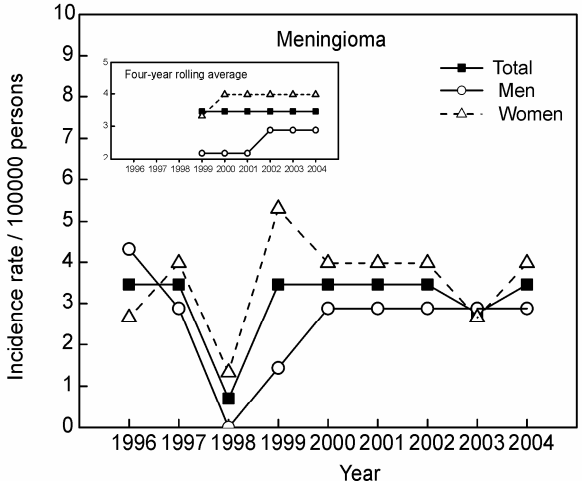

Meningioma
Four-year rolling average
Total
Men
Women
Incidence rate / 100000 persons
Year
1996 1997 1998 1999 2000 2001 2002 2003 2004

Figure 3. Annual incidence rates (*per* 100000 persons) of primary intracranical tumors in adult population (≥18 years of age) of the Varaždin County for the 1996-2004 period, overall and according to sex. Except for glioblastoma and meningioma, data for specific tumor types are not shown due to low incidence rates. Data are true (raw) incidence rates, and inserted boxes show "smoothed" (four-year rolling average) curves.