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Survival of patients with primary CNS tumours in Estonia

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Abstract

We studied a population-based survey that included 1417 patients with a primary central nervous system (CNS) tumour diagnosed in Estonia between 1986 and 1996. Survival rates at 1 and 5 years and median survival by histology and patient's age at diagnosis were estimated. Median survival time for all tumours was 33.2 months and 1- and 5-year survival rates were 59.3 and 46.0%, respectively. In multivariate analysis, younger age, better clinical condition (i.e. a Karnofsky Performance Status (KPS) score of 60 and more) and tumour histology were all dependent prognostic factors for better survival. Risk of death was more than 8 times greater for glioblastoma (Risk Ratio (RR) 8.31) and approximately seven times greater for anaplastic astrocytoma (RR 7.22) and other gliomas (RR 5.74) compared with meningiomas. Comparing the first (1986–1989) and the third (1994–1996) time periods, statistically significant improvements in survival occurred for all tumours and astrocytomas. Declines in survival during the second period (1990–1993) were statistically significant for all the tumour groups, but the most striking decrease took place in patients with glioblastoma. Age-specific rates showed that the increase in survival was more evident for patients aged between 45 and 64 years.

Keywords: Survival; CNS tumours; Estonia; Prognostic factors

1. Introduction

Most of the published studies concerning survival of central nervous system (CNS) tumours are hospital-based and restricted to gliomas or their histological subtypes. Very few population-based studies including survival of all primary benign and malignant tumours have been published. Increased mortality rates for malignant CNS tumours, particularly among the elderly, have been attributed to improved diagnostic techniques and increased environmental carcinogens [1]. A study from the Estonian Cancer Registry [2] reported the 5-year relative survival rate among patients of diagnosed CNS tumours in Estonia (1983–1987) as 11.2% for males and 24.6% for females and the mortality rate (1988–1992) as 4.9 and 3.5 per 100 000 population, respectively. Since meningiomas and other histologically benign CNS tumours were not recorded until 1998, the registry can be considered complete with regard to malignant tumours, but incomplete concerning benign tumours. In the recent EUROCARE survey [3], including malignant CNS tumours diagnosed between 1985 and 1989 in 17 European countries, the mean European age-standardised 5-year relative survival was 17% in men and 20% in women with markedly lower rates in Scotland, Estonia and Poland. In the USA in 1986–1991, 5-year relative survival of malignant CNS tumours was 20% according to the Surveillance, Epidemiology and End Results (SEER) data [4].

Generally, in CNS tumours, survival rates decline with increasing age at diagnosis. Other patient-related prognostic factors for survival are gender and the clinical condition of the patient. Histology and anatomical location are important tumour-related agents in estimating survival. The prognosis for patients with benign meningiomas is better for females and depends on the patient's age [5,6], being more favourable for patients below 60 years.

Clinically significant improvements in the survival of patients with CNS tumours has taken place over the last two decades [3,4]. Improvements in survival have been histology-specific, being more evident in medullo-

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blastomas, astrocytomas and oligodendrogliomas. For glioblastomas, the most frequent primary CNS tumour, no striking improvement has taken place.

The aim of this study was to determine the relative 1- and 5-year survival rates of patients with primary CNS tumours diagnosed in Estonia between 1986 and 1996, to examine variations in the different age and histological groups and evaluate changes in the length of survival that have occurred over recent years.

2. Patients and methods

2.1. Data collection and selection

The study was based on the Estonian population of approximately 1.5 million served by two neurosurgical centres (Tartu University Clinics and Tallinn Mustamäe Hospital) which admit all patients suspected of intracranial tumours. Our data included all cases of primary CNS tumours diagnosed at these hospitals from 1986 to 1996. We obtained information about patient's gender, age at diagnosis, clinical condition, tumour location, histological type and follow-up results from case histories, autopsy protocols and pathology reports. Additional information on date and cause of death was received from the Estonian Cancer Registry and the Estonian State Statistical Office.

We selected 1524 patients diagnosed between 1986 and 1996 with CNS tumours by using the International Classification of Diseases for Oncology (ICDO) [7] including the following topography codes: C71.0–C71.9 for brain, C70.0 and C70.9 for meninges, C72.2–C72.9 for cranial nerves and other intracranial parts of the CNS, C75.1–C75.3 for pituitary gland, pineal gland and craniopharyngeal duct. 88 cases discovered at autopsy, 2 patients of incomplete data and 17 patients diagnosed with another tumour previously or during the follow-up period were excluded.

2.2. Data classification

The remaining 1417 tumours were classified according to the histopathological type of the CNS tumour following the scheme approved by the World Health Organization (WHO) [8]. All histologically obscure cases (with the majority of pathological material having been preserved) were retrospectively overviewed by a neuropathologist. The study population was divided into four age groups: children ($\leqslant$20 years at diagnosis), younger adults (21–44 years), older adults (45–64 years) and the elderly ($\geqslant$65 years), reflecting the fact that CNS tumours have specific characteristics including histology, behaviour, anatomical location depending on age, and survival rates are varying by age at diagnosis. The clinical functional ability of the patient before therapy was assessed according to the Karnofsky Performance Status scale. Three groups were considered: score 80–100, 60–70 and less than 60.

2.3. Time periods

Our study included CNS tumours diagnosed in Estonia between 1986 and 1996. Follow-up of vital status was until 1 January 1998. Follow-up was based on the data of the Estonian Cancer Registry and the Estonian State Statistical Office.

To estimate potential changes in 1-year survival rates over time in the different age and histological groups, three time periods were defined according to the year of diagnosis: 1986–1989, 1990–1993 and 1994–1996. Advances in diagnostic procedures (the introduction of computerised tomography (CT) and magnetic resonance imaging (MRI)) should not affect potential changes in survival, as the first CT scan was introduced in 1983 in Estonia. Changes in 5-year survival were not estimated because of too short a follow-up period.

2.4. Data analysis

Survival time was calculated from the date of diagnosis. One- and 5-year survival rates were estimated overall, by the above-mentioned age groups, for each histological group using the life table method with intervals of 1 month. Kaplan–Meier estimation was used to compute the median length of survival by gender, age and clinical condition, histology and location of tumour, based on the whole study period. The logrank-test was used to compare survival in the subgroups. Proportional hazards models (Cox's models) were used to determine the effect of different patient (gender, age, clinical condition before treatment) and tumour-related (anatomical location, histology) factors on survival. All analyses were performed by using PC: SAS Version 6.12 (SAS Institute, Cary, NC, USA).

3. Results

3.1. General data

The 1417 patients included 628 men and 789 female with CNS tumours. The median age at referral was 49 years (range 1–83 years) for men and 52 years (range 4 months–84 years) for women.

The distribution and median survival of patients by gender, age, tumour location and clinical condition are shown in Table 1. Univariate analysis found that females ($P=0.002$), patients of younger age (<45 years, $P=0.0001$) and better clinical condition before treatment ($P=0.0001$) had the highest survival. Concerning tumour location, the worst prognosis was associated with those

Table 1
Characteristics of 1417 brain tumour patients diagnosed in Estonia from 1986 to 1996

Characteristic	Patients *n* (%)	*n* Deaths	Median survival (months)
Gender			
Male	629 (44.4)	371	18.6
Female	788 (55.6)	396	62.8
			$P=0.002$
Age group (years)			
⩽20	191 (13.5)	90	88.3
21–44	344 (24.3)	140	136.9
45–64	677 (47.8)	401	15.8
⩾65	205 (14.5)	136	5.7
			$P=0.0001$
Location			
Frontal	164 (11.6)	107	17.8
Parietal	113 (8.0)	63	14.7
Temporal	108 (7.6)	71	13.9
Two or more lobes	336 (23.7)	231	10.4
Central structures and ventricles	58 (4.1)	36	7.3
Other supratentorial	175 (12.4)	82	nc
Pituitary or pineal	114 (8.0)	28	nc
Infratentorial	311 (21.9)	133	nc
<Location not available	38 (2.7)		
			$P=0.0001$
KPS			
80–100	370 (26.1)	105	nc
60–70	558 (39.4)	289	48.0
<60	321 (22.7)	251	5.3
KPS not available	168 (11.9)		
			$P=0.0001$

nc, median could not be computed, over 50% survived; KPS, Karnofsky Performance Status.

of central structures or ventricular location and the best prognosis with infratentorial and pituitary location.

3.2. Distribution by histology

The distribution of tumours by histology according to the WHO classification of CNS tumours with the corresponding ICDO morphology codes are presented in Table 2. The most frequently reported histologies were glioblastoma (21.0%), meningioma (18.8%) and astrocytoma (9.2%).

3.3. Survival by histology

One- and 5-year survival rates and median survival time by histology are presented in Table 3. The overall 1-year survival was 59.3%, 5-year survival 46.0% and median survival 33.2 months. Tumours with the most favourable prognosis included pituitary adenoma (89.2%, both 1- and 5-year survival rates), meningioma (1-year survival 85.9% and 5-year survival 82.4%) and neurinoma (76.4%, both survival rates). Patients with glioblastoma and anaplastic astrocytoma had the worst outcome (5-year survival 8.6 and 15.8%, respectively). In contrast, approximately half of the low-grade astrocytoma patients (49.8%) survived beyond 5 years. The long-term prognosis for patients with medulloblastoma, ependymoma, oligodendroglioma and mixed gliomas appeared similar to each other (22.5, 26.9, 28.1 and 28.1%, respectively), while median survival was not so homogenous.

3.4. Survival by age at diagnosis

Survival rates by age at diagnosis for all CNS tumours and selected histology groups are given in Table 4. Including all histological groups, the worst outcome occurred in patients aged 65 years or older. Decreased survival associated with older age at diagnosis was generally observed in all histological groups. Differences were the most evident in the astrocytoma group (1-year survival 16.7% in the elderly and 87.0% in children, 5-year survival rates of 16.7 and 79.3%, respectively), where survival decreased with age.

3.5. Comparison of 1-year survival rates in the three time periods

Table 5 shows the 1-year survival rates for astrocytoma, glioblastoma, meningioma, tumours without histological verification and all tumours by patient age group during the three time periods (1986–1989,

Table 2
Distribution of CNS tumours by histology in Estonia (1986–1996)

Histology by WHO	ICDO Morphology Codes	Cases		
		n (%)	Male (%)	Female (%)
Tumours of neuroepithelial tissue				
Astrocytoma (G1–2)	9400/3, 9410/3, 9411/3, 9420/3, 9421/3	138 (9.2)	64 (10.2)	66 (8.4)
Anaplastic astrocytoma	9401/3	72 (5.6)	36 (5.7)	44 (5.6)
Glioblastoma	9440/3, 9441/3, 9442/3	297 (21.0)	159 (25.3)	138 (17.5)
Oligodendroglioma	9450/3	24 (1.7)	16 (2.5)	8 (1.0)
Anaplastic oligodendroglioma	9451/3	14 (0.9)	6 (1.0)	8 (1.0)
Ependymoma	9391/3, 9393/1	12 (0.8)	7 (1.1)	5 (0.6)
Anaplastic ependymoma	9392/3	10 (0.7)	6 (1.0)	4 (0.5)
Mixed gliomas	9382/3	23 (1.6)	11 (1.8)	12 (1.5)
Choroid plexus tumours	9390/0, 9390/3	9 (0.6)	6 (1.0)	3 (0.4)
Neuroepithelial tumours of uncertain origin	9430/3, 9443/3, 9381/3	12 (0.8)	4 (0.6)	8 (1.0)
Pineal tumours	9361/1, 9362/3	3 (0.2)	3 (0.5)	0 (0.0)
Medulloblastoma	9470/3, 9471/3, 9472/3	39 (2.8)	20 (3.2)	19 (2.4)
Tumours of cranial and spinal nerves				
Neurinoma	9560/0	55 (3.9)	18 (2.9)	37 (4.7)
Neurofibroma	9540, 9550/0	4 (0.3)	1 (0.2)	3 (0.4)
Tumours of the meninges				
Meningioma	9530/0, 9531/0, 9532/0, 9533/0, 9534/0, 9537/0, 9530/1, 9538/1	267 (18.8)	62 (9.9)	205 (26.0)
Anaplastic meningioma	9530/3	17 (1.2)	4 (0.6)	13 (1.6)
Haemangioblastoma	9161/3	21 (1.5)	8 (1.3)	13 (1.6)
Malignant lymphomas	9590/3	18 (1.3)	10 (1.6)	8 (1.0)
Germ cell tumours	9064/3, 9070/3, 9080/1, 9084/3	4 (0.3)	2 (0.3)	2 (0.3)
Cysts and tumour-like lesions	9084/0	9 (0.6)	7 (1.1)	2 (0.3)
Pituitary adenoma	8140/0	35 (2.5)	15 (2.4)	20 (2.5)
Pituitary carcinoma	8140/3	3 (0.2)	2 (0.3)	1 (0.1)
Craniopharyngioma	9350/1	15 (1.1)	8 (1.3)	7 (0.9)
All others	[a]	38 (2.7)	20 (3.2)	18 (2.3)
Unclassified tumours (no histological verification)	8000/0, 8010, 8000/1, 8001/1, 8000/3, 8001/3, 8002, 8003	278 (19.6)	134 (21.3)	144 (18.3)
Total		1417 (100)	628 (100)	789 (100)

WHO, World Health Organization.
[a] Amount of cases in each histological group was very small, morphology codes are not given.

Table 3
One- and 5-year survival rates (SR), and median survival time (ST) by histology for patients with primary brain tumours in Estonia (1986–1996)

Histology	*n*	1-year SR (%) (95% CI)	5-year SR (%) (95% CI)	Median ST (months)
Astrocytoma (G1–2)	138	64.5 (60.4–68.6)	49.8 (45.2–54.4)	54.2
Anaplastic astrocytoma	72	36.1 (30.4–41.8)	15.8 (11.3–20.4)	8.3
Glioblastoma	297	28.0 (25.4–30.6)	8.6 (6.8–10.3)	6.2
Ependymoma	22	50.0 (39.3–60.7)	26.9 (16.5–37.4)	10.7
Oligodendroglioma	38	60.5 (52.6–68.5)	28.1 (18.7–37.3)	22.9
Mixed gliomas	23	56.5 (46.2–66.9)	28.1 (18.2–37.9)	22.4
Medulloblastoma	39	53.9 (45.9–61.8)	22.5 (15.3–29.7)	12.7
Meningioma	284	85.9 (83.9–88.0)	82.4 (80.0–84.8)	nc
Neurinoma	55	76.4 (70.6–82.1)	76.4 (70.6–82.1)	nc
Pituitary adenoma	35	89.2 (78.4–94.3)	89.2 (78.4–94.3)	nc
Craniopharyngioma	15	73.3 (61.9–84.8)	52.4 (37.4–67.3)	nc
Other specified	121	62.6 (57.9–67.3)	43.8 (38.8–48.8)	36.5
Without histology	278	61.9 (59.0–64.8)	53.8 (50.7–56.8)	nc
Total	1417	59.3 (58.0-60.6)	46.0 (44.6-47.4)	33.2

95% CI, 95% confidence interval; nc, median could not be computed, over 50% survived.

1990–1993 and 1994–1996). Comparing the first (1986–1989) and the second (1990–1993) time periods, a statistically significant decline in the 1-year survival rate for glioblastoma (32.7 and 17.9%, respectively) and for all tumours (59.8 and 53.6%, respectively) was observed. In meningiomas, a similar result was evident only for those aged between 45 and 64 years. Comparing the first (1986–1989) and the third (1994–1996) time periods no significant changes in survival, either for meningioma or glioblastoma, have taken place. There were statistically significant improvements in the survival rates comparing the first (1986–1989) and the third (1994–1996) time periods for patients with astrocytoma and for all tumours. Age-specific rates showed that the increase in survival was more evident in the older adults, between 45 and 64 years, both, for all tumours (51.8% in 1986 through to 1989 and 64.8% in 1994 through to 1996) and for astrocytomas (29.4 and 83.3%, respectively). In patients with astrocytomas, a slight, but statistically not significant improvement can be observed in the younger adults, aged between 21 and 44 years.

3.6. Multivariate analysis

In multivariate analysis, older age at diagnosis, patient's clinical condition (Karnofsky Performance Status <60), tumour histology and period of diagnosis were independent prognostic factors for survival (Table 6). Risk of death was more than 8 times greater for glioblastoma (Risk Ratio (RR) 8.31, $P=0.0001$), about seven times greater for anaplastic astrocytoma (RR 7.22, $P=0.0001$) and more than 5 times greater for other gliomas (RR 5.74, $P=0.0001$). The best prognosis was found for those with neurinomas, but these patients still had a significantly greater risk of death (RR = 1.87, $P=0.0376$) compared with those with meningiomas.

4. Discussion

This analysis provides population-based survival estimates for both histologically benign and malignant CNS tumours in Estonia. One- and 5-year survival rates and the prognostic importance of patient- and tumour-related factors were analysed in 1417 patients with CNS tumours. The distribution of pathologically-confirmed cases according to histological type in Estonia is in many respects similar to the distribution reported for other geographical regions [6,9]. In our study, gliomas comprised 50% (including glioblastoma 21.0%, astrocytoma 14.8%), meningioma 20.0% and neurinoma 3.9% of all CNS tumours. A recent US study [10] based on the National Cancer Data Base (NCDB), a data set that is limited to hospital reporting, has found approxi-

Table 4
One- and 5-year survival rates (SR) by age at diagnosis for selected histology groups

Histology	Age at diagnosis					
	⩽20			21–44		
	n	1-year SR (95% CI)	5-year SR (95% CI)	*n*	1-year SR (95% CI)	5-year SR (95% CI)
Astrocytoma (G1–2)	46	87.0 (82.0–91.9)	79.3 (73.1–85.6)	43	76.7 (70.3–83.2)	64.6 (56.8–72.5)
Anaplastic astrocytoma	4	[a]	[a]	21	52.4 (41.5–63.3)	26.8 (16.8–36.8)
Glioblastoma	12	41.7 (27.5–55.9)	21.6 (8.9–34.3)	55	43.6 (37.0–50.3)	13.8 (8.6–19.0)
Other glioma	13	76.9 (65.2–88.6)	46.2 (30.3–62.0)	30	63.3 (54.5–72.1)	40.8 (30.8–50.8)
Meningioma	3	[a]	[a]	58	93.1 (89.8–96.4)	93.1 (89.8–96.4)
Neurinoma	5	[a]	[a]	18	88.9 (81.5–96.3)	88.9 (81.5–96.3)
Other specified	65	58.5 (52.4–64.6)	35.6 (29.3–41.8)	53	87.8 (83.1–92.4)	77.1 (70.6–83.6)
Without histology	43	69.8 (62.8–76.8)	55.3 (47.6–62.9)	66	81.8 (77.1–86.6)	72.8 (67.1–78.6)
Total	191	70.2 (66.9–73.5)	52.9 (49.1–56.6)	344	74.7 (72.4–77.1)	60.9 (58.1–63.7)
	45–64			⩾65		
	n	1-year SR (95% CI)	5-year SR (95% CI)	*n*	1-year SR (95% CI)	5-year SR (95% CI)
Astrocytoma (G1–2)	37	37.8 (29.9–45.8)	13.2 (6.2–20.3)	12	16.7 (5.9–27.4)	16.7 (5.9–27.4)
Anaplastic astrocytoma	39	25.6 (18.7–32.6)	8.6 (3.6–13.5)	8	[a]	[a]
Glioblastoma	173	24.3 (21.0–27.5)	6.3 (4.3–8.3)	57	21.1 (16.6–26.5)	7.0 (3.6–10.4)
Other glioma	31	51.6 (42.6–60.6)	18.3 (11.2–25.4)	9	[a]	[a]
Meningioma	182	83.5 (80.8–86.3)	79.8 (76.7–82.9)	41	85.4 (79.9–90.9)	75.0 (66.6–83.4)
Neurinoma	23	73.9 (64.8–83.1)	73.9 (64.8–83.1)	9	[a]	[a]
Other specified	79	59.5 (54.0—65.0)	44.8 (38.9–50.6)	13	46.2 (32.4–60.0)	30.8 (18.0–43.6)
Without histology	113	56.6 (52.0–61.3)	49.0 (44.2–53.9)	56	42.9 (36.3–49.5)	39.3 (32.7–45.8)
Total	677	53.5 (51.6–55.4)	40.7 (38.7–42.6)	205	42.4 (39.0–45.9)	32.3 (28.9–35.8)

95% CI, 95% confidence interval.
[a] Not given due to a very small number (<10) of cases.

Table 5
1-year survival rates (SR) by age for patients with low-grade astrocytoma, glioblastoma, meningioma and without histological confirmation and all brain tumours during the three time periods. Estonia 1986–1996

Histology	Age group (years)	Year of diagnosis		
		1986–1989 SR (95% CI)	1990–1993 SR (95% CI)	1994–1996 SR (95% CI)
Astrocytoma (G1–2)	⩽20	88.2 (80.8–96.1)	81.3 (71.5–91.0)	92.3 (84.9–99.7)
	21–44	76.5 (66.2–86.8)	58.3 (44.1–72.6)	92.9 (86.0–99.7)
	45–64	29.4 (18.4–40.5)	28.6 (16.5–40.6)	83.3 (68.1–98.5)
	⩾65	25.0 (3.4–46.7)	[a]	[a]
	All ages	61.8 (55.3–68.4)	54.6 (47.0–62.1)	79.5 (73.0–86.0)
Glioblastoma	⩽20	[a]	[a]	[a]
	21–44	45.0 (33.9–56.1)	22.2 (12.4–32.0)	52.9 (40.8–65.1)
	45–64	27.1 (21.8–32.5)	17.1 (12.6–21.6)	33.3 (25.1–41.5)
	⩾65	25.0 (14.2–35.8)	9.1 (3.0–15.2)	31.6 (20.9–42.2)
	All ages	32.7 (28.2–37.2)	17.9 (14.2–21.5)	36.0 (30.5–41.5)
Meningioma	⩽20	[a]	[a]	[a]
	21–44	90.5 (84.1–96.9)	95.8 (91.7–99.9)	92.3 (84.9–99.7)
	45–64	86.0 (81.4–90.6)	74.6 (69.1–80.1)	90.3 (86.6–94.1)
	⩾65	[a]	84.6 (74.6–94.6)	81.8 (73.6–90.0)
	All ages	88.1 (84.6–91.6)	81.2 (77.3–85.1)	88.9 (85.7–92.1)
Without histology	⩽20	57.9 (46.6–69.2)	71.4 (58.7–83.5)	90.0 (80.5–99.5)
	21–44	87.5 (80.8–94.3)	83.3 (72.6–94-1)	76.7 (69.0–84.4)
	45–64	52.5 (44.6–60.4)	67.7 (59.3–76.1)	52.4 (44.7–60.1)
	⩾65	69.2 (56.4–82.0)	31.8 (21.9–41.8)	38.1 (27.5–48.7)
	All ages	64.6 (59.7–69.5)	60.8 (55.3–66.3)	60.2 (55.4–65.0)
Total	⩽20	65.7 (59.9–71.5)	72.5 (67.1–77.8)	72.7 (66.7–78.7)
	21–44	78.1 (74.3–81.8)	69.4 (65.0–73.9)	76.1 (72.1–80.1)
	45–64	51.8 (48.6–55.0)	46.0 (40.3–49.2)	64.8 (61.3–68.2)
	⩾65	47.1 (44.8–54.1)	37.0 (31.3–42.6)	44.4 (38.9–50.0)
	All ages	59.8 (57.6–62.1)	53.6 (51.3–55.9)	64.9 (62.7–67.2)

95% CI, 95% confidence interval.
[a] Not given due a very small number of cases.

Table 6
Multivariate analysis (Cox model). Factors predicting survival in patients with brain tumours

Factor	Variable	Parameter estimate	*P* value	Risk ratio (in best Cox model)
Gender	Male versus female		ns	1.02
Age (years)	as a continuous variable	0.014	0.0001	
Karnofsky Performance Status				
<60%	60–100% taken as a base category	0.600	0.0001	1.82
Not specified		0.552	0.0001	1.74
Period of diagnosis				
1990–1993	1986–1989 taken as a base category		ns	
1994–1996		−0.190	0.0280	0.83
Histology				
Astrocytoma	Meningioma taken as a base	1.429	0.0001	4.18
Anaplastic astrocytoma	category for all types	1.977	0.0001	7.22
Glioblastoma		2.117	0.0001	8.31
Other gliomas		1.748	0.0001	5.74
Neurinoma		0.624	0.0376	1.87
Other specified		1.497	0.0001	4.47
Without histology		1.166	0.0001	3.21
Localisation				
Hemispheres	Infratentorial location taken as		ns	
Central structures	a base category		ns	
Other			ns	
Not specified		1.461	0.0001	4.31

ns, non significant.

mately the same distribution concerning astrocytoma (18.7%), with a lower occurrence of meningioma (15.5%) and higher occurrence of glioblastoma (29.6%).

Gender differences in survival have previously been reported for non-malignant CNS tumours [5,6,11]. The prognosis for patients with benign meningiomas is better for females below 60 years of age [11,12]. The cause of this difference is unknown.

Most authors report no association between prognosis and patient gender in malignant CNS tumours [13,14].

In our series, including all CNS tumours, survival is considerably longer among females: median survival 62.8 months compared with only 18.6 months for males. This difference can be explained by the variations in the histologial distribution in men and women. There is a higher incidence of benign meningiomas in females together with a better prognosis for this type of tumour. The poorer survival of men is attributable to the relatively greater frequency among men of the more aggressive tumour types. In multivariate analysis, no difference in prognosis could be detected for male and female patients.

The importance of age and histology in predicting the survival from CNS tumours has been well documented in studies from the US [4,11,15–19], as well as studies from other countries [6,13,20,21]. Generally, survival rates decline with increasing age at diagnosis, both in benign and malignant tumours. A similar pattern was found in our study. The survival pattern of patients aged 45–64 years has been reported to resemble more closely that of older rather than younger patients [22]. However, some authors suggest that the influence of age is overestimated. Shaw and colleagues [23] suggest that the patient's age is not correlated with an improved survival in mixed gliomas.

In low-grade astrocytomas, the median survival time is reported to be approximately 5 years, similar to our result of 4.5 years (54.2 months). Long-term survival rates at 5 years have been documented as ranging between 30 and 60% [6,10,24], depending primarily on the inclusion criteria and study design. A hospital-based study of the NCDB [10] including over 60 000 patients with a CNS tumour, found 5-year survival rates of 30.3% for astrocytoma and 77.4% for pilocytic astrocytoma. Our data show 5-year survival rates of 49.8% for low-grade astrocytomas.

The overall median survival of grade 3 and 4 astrocytomas in our study was less than 1 year. However, Salcman and colleagues [17] reported that the median survival of grade 3 and 4 astrocytomas for patients less than 40 years of age, who received some form of therapy beyond surgery and radiation, was more than 2 years. Furthermore, younger patients with grade 3 astrocytomas generally have a better survival, extending over 4 years [25]. A Finnish study [13] reported the median survival of grade 3 and 4 gliomas to be 24.0 and 7.7 months, respectively. Barker and co-authors [15] reported a median survival rate of glioblastoma patients of 11.2 months, and 1- and 5-year survival rates of 48 and 4%, respectively. Our study determined a similar median survival rate for glioblastoma of 6.2 months and for anaplastic astrocytoma of 8.3 months, together with 1-year survival rates of 28.0 and 36.1% and 5-year survival rates of 8.6 and 15.8%, respectively. These data suggest patients had a poorer outcome than in other studies, especially those with anaplastic astrocytomas. The relative poor median survival of patients with anaplastic astrocytoma may be explained by difficulties in making this histological diagnosis. The biggest divergence in the results of neuropathologists lies in the diagnosis of anaplastic astrocytoma.

In oligodendrogliomas, the median survival time has been reported to be between 3 and 8 years [14,26,27]. Our data show patients had a survival rate of approximately 2 years, which is significantly lower, but comparable with the median survival of non-irradiated patients (26.5 months) in a Norwegian study [26]. Although patients with benign tumours have a more favourable prognosis compared with patients with malignant tumours, there is still significant mortality associated with these histologies. In our study, both the 1- and 5-year survival rates for meningiomas was approximately the same as those reported in the Finnish study [12] (83 and 79%, respectively). The Norwegian study reported survival following the dignosis of benign meningiomas to be 93% at 1 year and 95% at 5 years [5]. The US study [11], based on 9000 meningioma cases, found a 5-year survival rate of 69%. The clinical functional ability or Karnofsky score of the CNS tumour patient has been shown to be a strong predictor of outcome in most studies [14–16,18,23,28]. In our study, the patient's clinical condition was a statistically significant prognostic factor in both univariate and multivariate analyses.

Of course, appropriate therapies are among the main determinants of prognosis. The better outcome in the socio-economically advanced societies is due to earlier diagnosis and the combined effect of more effective therapies, including centralisation of treatment and dissemination of effective therapeutic protocols. In Estonia, the first CT scan was introduced in 1983 and MRI scans in early 1990s. Up to the present day, joint treatment protocols for patients with CNS tumours are lacking in Estonia. In this study, we did not investigate the association between treatment strategies and outcome. We suppose that in most cases only surgery, possibly a gross total resection was used. Post-operative radiation therapy and adjuvant chemotherapy or a combination is for certain reasons (e.g. the lack of defined treatment protocols and insufficient co-operation between surgeons and oncologists) not so widely used in Estonia.

4.1. Changes in incidence rates

During the last 20 years an overall slight increase in survival of patients with malignant tumours has been found both in EUROCARE study [3] and SEER programme [4]. Most improvement is confined to the first year after diagnosis. Age-specific rates show that the increase is more evident in younger patients, up to 54 years of age. Concerning tumour histology, the improvement is evident in medulloblastomas, in adults with astrocytomas and oligodendrogliomas [29]. The improvements in survival reflect improvements in therapy and the treatment taking place at an earlier stage of disease, where new and better diagnostic techniques have helped in identifying the tumours earlier.

In meningiomas, both short-term and long-term survival has recently improved [5]. The improved 1-year survival rate is likely to be caused by improved operative techniques and postoperative care. The increased long-term survival may reflect the likelihood that more patients with small meningiomas are being diagnosed early since CT became available. In benign meningiomas, a small tumour size is one of the factors independently associated with an increased survival time [11].

Our survey follows the example of above-mentioned studies, statistically significant improvements in 1-year survival rates were found for all tumours and low-grade astrocytoma comparing the first and the third time periods. Age-specific rates showed that the increase was more evident in patients aged between 45 and 64 years. A decline in survival during the second period (1990–1993) is statistically significant for all tumours, but the most striking decrease took place for patients with glioblastoma. This discrepancy may reflect economic factors and the reorganisation of the health care system at the beginning of the 1990s. It was a period of extensive change in Estonia, in both the political and economical systems, including healthcare. Delays in diagnosis, especially in rural areas where availability of medical care was limited, may also have caused the poorer outcome during the second period. Older patients are also more likely to be diagnosed as having dementia or vascular disease by their family doctors than as having CNS tumours.

In conclusion, the outcome of CNS tumours in Estonia, especially malignant tumours, is somewhat worse compared with other studies. The causes of such a tendency, especially with regard to treatment strategies, deserves further investigation.

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