Epidemiology and outcome research of glioma patients in Southern Switzerland: A population based analysis

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Abstract

A proper observation of epidemiology and therapeutic outcome of patients with glial tumours is crucial for treatment selection, and planning of adequate territorial and environmental interventions. A glioma working group has been assembled in our region, in order to study this particular type of cancer We reviewed epidemiology and clinical data of glioma patients followed in our region over a 9-year period (1996-2004). The population-based analysis was made collecting relevant data from Ticino Cancer Registry (TCR) and the clinical files from our departments of Neurosurgery (NS), Medical Oncology (MO), Radiation Oncology (RO) and Pathology. Descriptive statistical analysis and incidence rates are provided. The total number of glioma patients was 175 (M 93, F 65). Annual incidence was 5.8/100'000/yr (M 7.0, F 4.8). A certain increase of incidence was detected over observation time. Main histology subtypes were: Astrocytoma 147 (93%), Oligodendroglioma 5 (3%), Oligoastrocytoma 3 (1.8%), Ependimoma 3 (1.8). For the whole population the median survival time was 12.17 months (95% CI 9.64 – 14.69). Grade 4 cases showed the worst survival (median survival time: 7.93) and only one Grade 1 case deceased in the observed period. Analysis of treatment influence on outcome and complication rate of treatments are now under evaluation and will be the subject of further publication.
As a conclusion, this evaluation confirms survival data reported from literature. Glioma incidence in our region is consistent with the pattern of Western Europe. We have found that teamwork with co-operation of different departments and relationships with other institutions in other Swiss regions and other countries plays a key role for an optimal treatment of these patients.

Introduction

Tumours of the Central Nervous System are relatively uncommon, representing the 2-3% of the causes of death due to malignancy (1-2). Even if it is quite a rare disease, it has to be considered with special attention in consideration of its important impact on neurological function, particularly in the case of patients with malignant astrocytomas, who frequently experience a reduced quality of life and severe impairment of social and familiar integrity (1-5).
The more frequent brain tumours are brain metastases and malignant gliomas (1). The former are generally studied and treated in the context of systemic disease. Primary neoplasms of the central nervous system, and mainly gliomas, constitute a sort of disease with peculiar clinical and epidemiologic aspects that need to be studied separately. The age distribution of gliomas is bimodal, with a peak incidence in children and a second larger peak in adults aged over 45 (7). Geographical variation in incidence is less than for other human neoplasms, however tends to be higher in more developed countries. In North America and Europe incidence rates are between 6-8 new cases per 100.000 individuals per year.
A proper observation of epidemiology and therapeutic outcome of patients with glial tumours is crucial in order to better select the treatment options, mainly those directed to the patients who bear high grade tumours, but also for those with low grade gliomas. Furthermore, it is very important to compare disease incidence and treatment outcome with what is reported by others, in order to identify unexpected incidences related to environment, social status and other risk factors, as well as to improve diagnostic and therapeutic strategies.
A glioma working group has been organised in our region, in order to study this particular type of cancer. This co-operative group is composed of the departments of Neurosurgery, Radiation Oncology, Medical Oncology, the Cantonal Institute of Pathology and the Ticino Cancer Registry. On a regular basis clinical cases are discussed in dedicated neuro-oncology tumour boards; moreover the clinical activity is supported by epidemiologists and pathologists.
We herewith report the first data set of epidemiology and survival of glioma patients in Canton Ticino.The present analysis will be also the basis for further discussion on this topic.

Patients and methods

A review of epidemiology and clinical data of glioma patients followed in our region was done over a 9-year period (1996-2004). The population based analysis was made collecting relevant data from the Ticino Cancer Registry (TCR) and the clinical

Tab. 1. Number of cases by sex

Year of diagnosis	Males	Females	Total
1996	5	10	15
1997	8	4	12
1998	21	5	26
1999	8	11	19
2000	7	10	17
2001	11	10	21
2002	19	4	23
2003	9	10	19
2004	13	10	23
Total	**101**	**74**	**175**

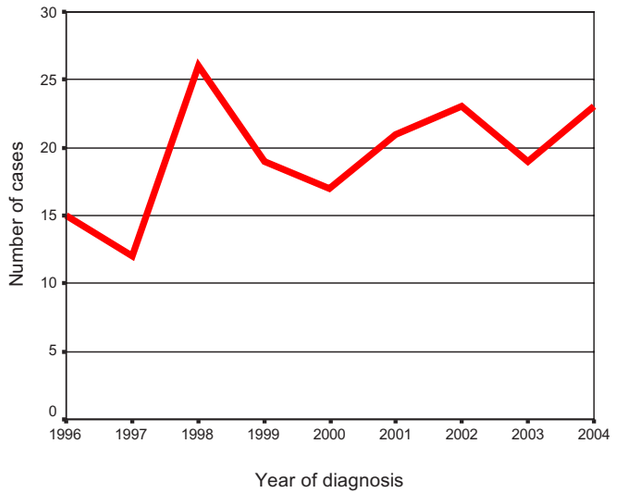

Fig. 1. Number of cases by year of diagnosis

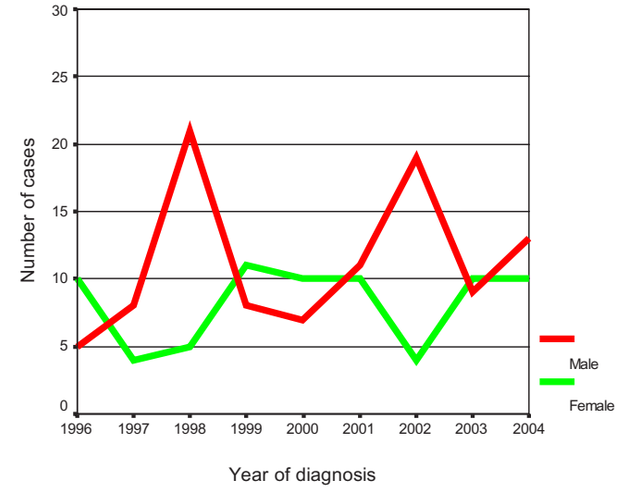

Fig. 2. Number of cases by sex and year of diagnosis

files from our departments of Neurosurgery (NS), Medical Oncology (MO) and Radiation Oncology (RO) of Canton Ticino (Switzerland) and the Cantonal Institute of Pathology (ICP). Gliomas are classified in TCR and ICP following the directive of WHO blue book (2) and coded with ICD-O-III (6). For data collection the TCR uses the WHO directive (for more details see www.ti.ch/cancer).

Statistical Considerations

Descriptive statistical analysis and incidence rates are provided. Survival analysis was performed by statistical methodology applied in that generally used to analyse survival time data and the time endpoint of interest was date of death. Overall survival was calculated from date of diagnosis until death or last follow-up update (right censoring). Survival curves were generated using the Kaplan-Meier method and differences in survival functions between groups were assessed by way of the log-rank test (LRT) (Kaplan & Meier, 1958). Analyses were carried out using SPSS biostatistical package.

Results

According to the data of the TCR from 1996 to 2004 the total number of glioma patients was 175 (M 93, F 65). Annual incidence was 5.8/100.000/yr (M 7.0, F 4.8). A certain increase of incidence was detected over observation time, with no difference for sex (**Fig. 1 and 2**). The age distribution is plotted on **Fig. 3**; the majority of the cases were observed in aged population (50-70 yrs), with the lower incidence in the paediatric subset of patients. The percent of different WHO grade is reported in **Fig. 4** being WHO I: 4.0%, WHO II: 14.9%, WHO III: 6.9%, WHO IV: 56.0%. Main histology subtypes were: Astrocytoma 147 (93%), Oligodendroglioma 5 (3%), Oligoastrocytoma 3 (1.8%), Ependimoma 3 (1.8).

Details of survival analysis are reported in **Tab. 2** and graphical view is displayed in **Figs. 5-8**. For the

whole population the median survival time was 12.17 months (95% CI 9.64 – 14.69) (**Fig. 5**). No statistically significant differences have been observed between sexes (LRT=0.47; p=0.495) (**Fig. 6**). A statistically significant difference haves been observed among WHO grades (LRT=31.89; p<0.001) (**Fig. 7**), as Grade 4 cases showed the worst survival experience (median survival time: 7.93) and only one Grade 1 case deceased in the observed period. Finally, a significant difference in survival does exist when astrocytoma cases are compared to other cases: median survival 63.6 vs 10.33 (LRT=5.59, p<0.05).
Information of treatment after diagnosis of glioma was routinely collected by the TCR only since 01.01.2003 (**Fig. 9**). Analysis of treatment influence on outcome and complication rate of treatments are now under evaluation and will be the subject of further publication.

Discussion

Incidence rates for malignant tumours of the central nervous system in Ticino seems to be equal in this estimate for Europe and North America. A bimodal incidence peak, one in children and the other in adults, is also present in Ticino as described in the literature.
Our evaluation confirms the data from literature that HGG has a poor outcome and that better treatment options are needed. LGG patients have a better prognostic profile, with longer survival, nonetheless in the majority of the cases these patients have quality of life and survival affected by their disease and treatment complications (5,8).
Both for malignant and low grade glioma patients, epilepsy, neurological and neuro-psychological impairment are specific problems needing particular commitment both at bedside and in research, including epidemiology, in order to identify better treatment options, unexpected complications of therapies. This will account for anti-cancer therapies, but

Tab. 2. Univariate survival analysis of glioma cases diagnosed during the period 1996-2000 (follow-up update 31.12.2004)

Variable	*Categories*	*Events*	*Censored*	*Median survival (months)*	*Log-rank test*	*p-value*
Overall		68	21	12.17		
Morphology	Astrocytomas	61	14	10.33	5.59	0.018
	Others	7	7	68.60		
Gender	Female	30	10	10.33	0.47	0.495
	Male	38	11	12.83		
Grade	I	1	5	-	31.89	<0.001
	II	8	7	77.53		
	III	2	2	12.47		
	IV	45	3	7.93		
	Indeterminate	12	4	6.63		

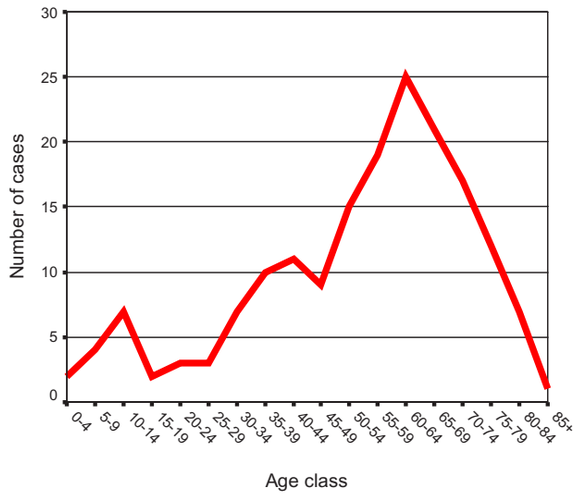

Fig. 3. Number of cases by age class

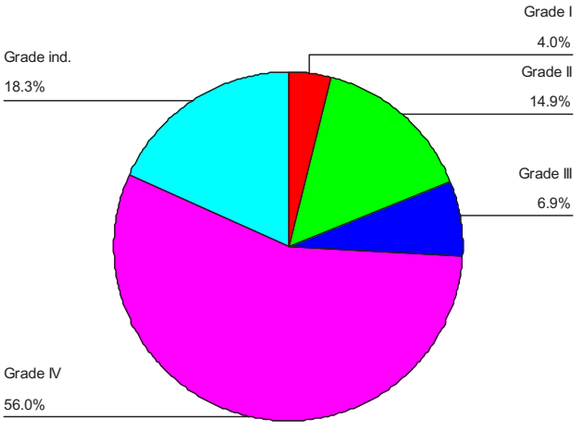

Fig. 4. Number of cases by WHO grade

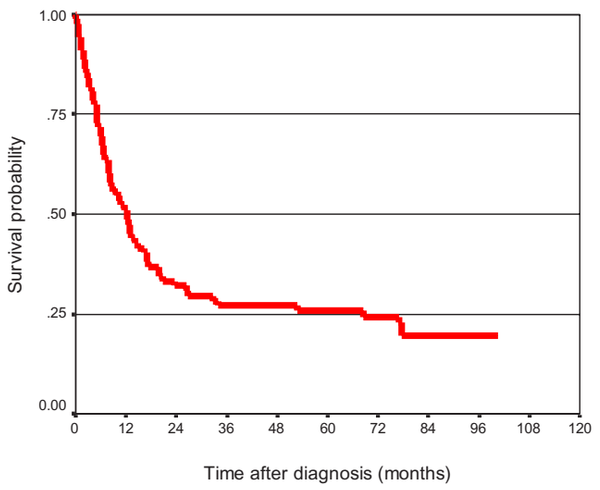

Fig. 5. Overall survival (Kaplan-Meier)

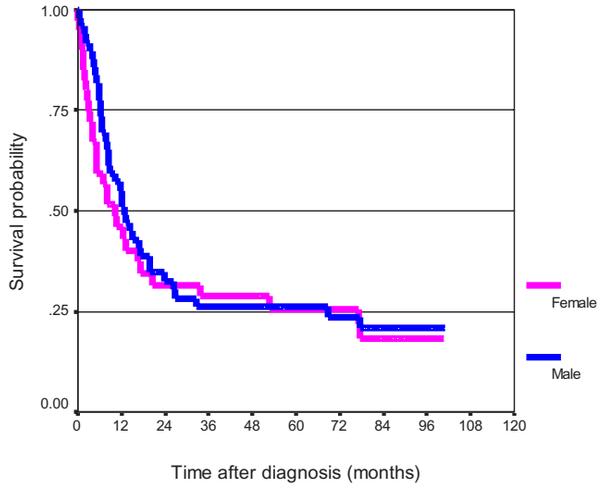

Fig. 6. Overall survival (Kaplan-Meier) by sex

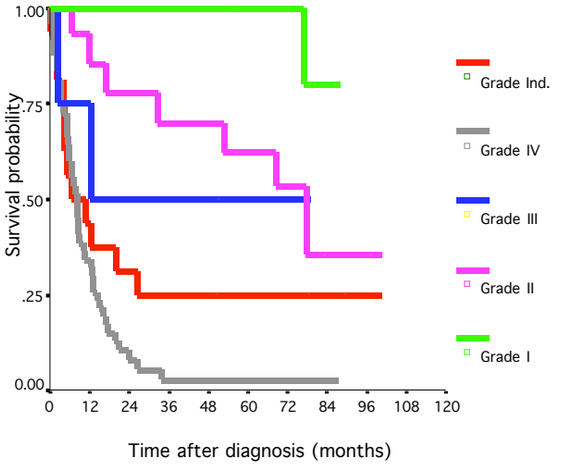

Fig. 7. Overall survival (Kaplan-Meier) by grade

also for supportive care drugs as steroids and anti-epileptic drugs, which frequently show an excess of toxicity, when combined with anti-tumoral agents and/or radiation (3). A further reason to invest time and ressources in the field of primary brain tumours, is given by the emerging role of therapies targeted to specific bio-molecular markers of gliomas, which seem to outline for the future different modalities of treatment for different molecular settings, with different prognostic profiles (4, 9-10). It will be necessary to continue to carefully investigate these diseases with special attention to old and new aspects.

Our team work with co-operation of different departments played a key role for an optimal management of such difficult diseases. Confrontation with other institutions in different countries confirms the importance of multidisciplinary approach in neuro-oncology. There is also some report in the dedicated literature which points out that coordinating the treatment of patients bearing brain neoplasms by specialised neuro-oncologists does ameliorate their outcome (11).

Finally, it is by most emphasized treating patients in the context of international, multi-institutional trials, in order to warrant best treatment options and contribute to clinical research. A recent EORTC trial on glioblastoma represents an example of the efficacy of multi-institutional cooperation, with rapid accrual and quick answers; as a result for the first time in the last 30 years a step forward has been done, demonstrating advantage in survival of the patients treated in the experimental arm (12). We regularly try to treat glioma patients in the context of multicenter controlled clinical trials to warrant them the best therapeutic options and also to contribute to clinical research in this subset of oncology. This attitude also requires adequate knowledge of the characteristics of our patient's population.

The Ticino Cancer Registry will contribute to this effort with continued data management and evaluation in

order to better understand the peculiarity of this type of cancer.
In order to rationalise work procedure, a common database is under discussion.

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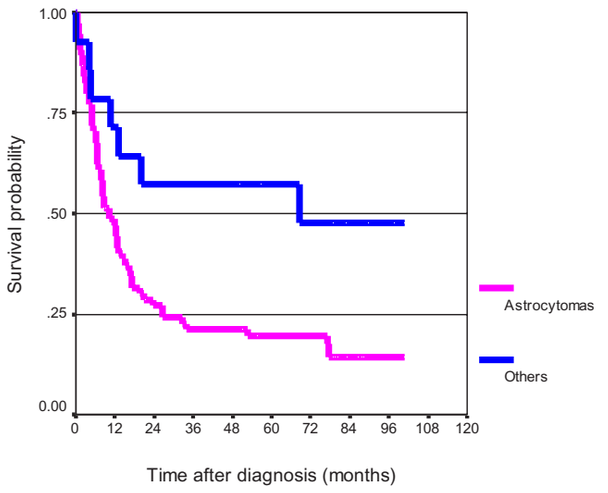

Fig. 8. Overall survival (Kaplan-Meier) by morphology

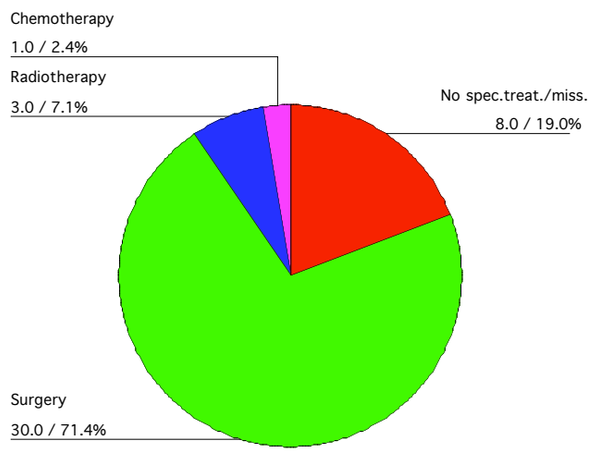

Fig. 9. First treament after glioma diagnosis (2003-2004)