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Clinical prognostic factors in adults with astrocytoma: Historic cohort

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ABSTRACT

Objective: To explore the clinical prognostic factors for adults affected with astrocytoma.
Patients and methods: Using a historic cohort, we selected 155 clinical files from patients with astrocytoma using simple randomization. The main outcome variable was overall survival time. To identify clinical prognostic factors, we used bivariate analysis, Kaplan Meier, the log rank test and the Cox regression models. The number of lost years lived with disability (DALY) based on prevalence, was calculated.
Results: The mean age at diagnosis was 45.7 years. Analysis according to tumour stage, including grades II, III and IV, also showed a younger age of presentation. Kaplan-Meier survival estimates showed that tumour grade, Karnofsky status (KPS) ≥70, resection type, chemotherapy, radiotherapy, alcohol consumption, familial history of cancer and clinical presentation were significantly associated with survival time. Using a proportional hazard model, age, grade IV, resection, chemotherapy + radiotherapy and KPS were identified as prognostic factors.The amount of life lost due to premature death in this population was 28 years.
Conclusion: In our study, astrocytoma was diagnosed in young adults. The overall survival was 15 months, 9% (n = 14) of patients presented a survival of 2 years, and 3% of patients survived 3 years. On average the number of years lost due to premature death and disability was 28.53 years.

1. Introduction

Cancer prognoses have significantly improved over the past 40 years. For instance, in 1975, the 5-year overall survival (OS) rates for breast and prostate cancer were 75% and 68%; currently, these rates are 90% and nearly 100%, respectively [1]. However,, the 5- year OS rate has increased by only 13% (22–35%) for central nervous system (CNS) tumours [1].

Malignant CNS tumours disproportionately contribute to cancer mortality, especially for high-risk age groups. In the USA, such tumours are the second and fifth leading causes of cancer mortality in men and woman, respectively, aged 20–39 years [2]. In Mexico brain tumour represent 2.8% of the mortality due to neoplasms and exhibited an incidence of 3.5 per 100,000 habitants in 2014 [3].

Astrocytomas are the most common and lethal CNS tumours, and the majority of these tumours are classified as grade IV (glioblastoma) (4.37 per 100,000 individuals) [2]. The OS for astrocytomas is 15 months despite the best treatment available, and only approximately 2% of all glioblastoma patients survive longer than 36 months [4].

The prognosis for astrocytomas can be predicted using specific clinical factors, which allow neurosurgeons and neuro-oncologists

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to define the best treatment for each patient. Certain patient features, such as age, gender, performance status and tumour localization, have been studied as potential prognostic factors [5]. However, few studies have reported demographic and clinical characteristics and prognostic factors in adult patients in Mexico [6–8].

The aim of this study was to explore the clinical and sociodemographic variables that affect OS in adult Mexican astrocytoma patients.

2. Patients and methods

2.1. Design

Study design. For this historical cohort, we used data from the National Institute of Neurology and Neurosurgery of Mexico (NINN) (Instituto Nacional de Neurología y Neurocirugía of México) from 2008 to 2014. The NINN is a national referral centre that receives patients from all geographic areas of the country. Clinical data were collected from pathological astrocytoma diagnoses until the time of death or last appointment.

Setting. The data featured 1100 patients diagnosed with a tumour of the central nervous system (CNS). Studies have reported that 33% of tumours treated at the NINN are gliomas [6]. The data show a confidence level of 95%, precision of 5% and proportion of at least 12% of surviving patients at two years of follow-up [9]. Three hundred records, were selected by simple randomization: from these, 155 patients who met the criteria for eligibility were included in the data analyses. The total CNS tumours and approximately 43% of all gliomas treated at the NINN during 7 years.

Eligibility criteria. Diagnoses of astrocytoma were confirmed by a certified pathologist; all individuals were naive to treatment and elected to receive diagnostic, therapeutic or surgical care. Other gliomas, tumours with components of other gliomas and metastases were excluded. All patients included were adults, more than 18 years old).

2.2. Variables

All variables were collected from clinical files. The main outcome variable was overall survival, which was defined as the time between diagnosis and the time of death or last appointment. The time of diagnosis was considered the date of surgery. The time of death was taken from the death certificate or active surveillance. Additionally, demographic and clinical data were collected and analysed; these variables were defined and used as follows. The tumour grade was determined by a certificated pathologist, who is an expert in neuro-diagnosis based on the World Health Organization (WHO) criteria [10]. The degree of resection was based on computed tomography (CT) or magnetic resonance imaging (MRI) results. The familial history of cancer was determined from the clinical file. Alcohol consumption, smoking history and comorbidities were self-reported in the clinical file. The Karnofsky status (KPS) was dichotomized as $\geq$70 and <70 based on work from Ewelt et al., who retrospectively analysed a large cohort of elderly glioblastoma multiform (GBM) patients and found that a preoperative KPS score ~70 was associated with significant survival benefits [11]. Socio-economic status was studied and classified by a social worker; personal and familial income, expenses, occupation, type of dwelling and health status were considered (a score of 1–2 represents low class, 3–4 represents medium class, and 5–6 represents high class). Body mass index (BMI) was classified based on the WHO parameters. Clinical presentation was considered the main characteristic that led the patient to seek treatment.

The number of potential years of healthy life lost to premature death was calculated by subtracting the actual age at the time of death from the of life expectancy reported for Mexico (women, 77 years and men, 72 years). The number of disability-adjusted life years (DALYs) was based on prevalence. It was obtained by multiplying the expected duration of disability (until remission or death) by a disability weight reflecting the average severity of the disease compared to individuals with perfect health and those who had died. We used specific disability weights for age and, treatment for form as of sequelae included in the Global Burden of Disease study.

Table 1
Demographical and clinical characteristics.

n = 155	n (%)
Demografic variables	
Age*	45.7 ± 15.1
Sex	
Female	68 (46)
Male	87 (56)
Socio-economic status	
Low class	121 (78)
Medium class	30 (19.4)
High class	4 (16.7)
Marital status	
Single	45 (29)
Common low marriage	26 (16.7)
Marriage	60 (38.7)
Divorce	14 (9.1)
Widower	10 (6.5)
Clinical variables	
BMI	
Malnutrition	2 (1.3)
Normal	70 (45.2)
Overweight	60 (38.7)
Obese	23 (14.8)
Morbility	
Previews neoplasia	9 (5.8)
Diabetes Mellitus 2	11 (7)
Hypertension	20 (13)
History of smoking	55 (35.5)
History of alcoholism	23 (14.8)

* = years.

2.3. Statistical analysis

The demographic and clinical characteristics of the subjects were summarized and reported. The bivariate analysis was generated using independent-sample Chi square or student's *t*-tests according to the type of variable, with comparisons between patients who were living and deceased. The effect of each measured factor on time to death was identified using Kaplan Meier curves Cox, regression models, and log rank tests and were used to identify differences in survival function between subgroups. A value of $p \leq 0.05$ was considered statistically significant. All analyses were performed using SPSS v21 and STATA 12.

2.4. Ethics

The NINN Ethical Committee on human experimentation approved the use of the human subject information included in this study. Internal codes were used to preserve patient confidentiality.

3. Results

3.1. Demographical characteristics

In total, 155 patients with astrocytomas were included in the analysis. The demographic data are shown in Table 1. The mean age at diagnosis was 45.7 ± 15.1 years, and a familial history of