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Changing incidence and improved survival of gliomas

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Abstract ***Background:*** Tumours of the central nervous system (CNS) represent a relatively rare but serious health burden. This study provides insight into the incidence and survival patterns of gliomas in the Netherlands diagnosed in adult patients during the time period 1989–2010, with a focus on glioblastoma and low-grade gliomas.
Methods: Data on 21,085 gliomas (excluding grade I tumours) were obtained from the Netherlands Cancer Registry, including tumours of the CNS without pathological confirmation. We calculated the age-standardised incidence rates and the estimated annual percentage change (EAPC) for all glioma subtypes. Crude and relative survival rates were estimated using information on the vital status obtained from the Dutch Municipal Personal Records Database.
Results: Incidence of gliomas in adults increased over time, from 4.9 per 100,000 in 1989 to 5.9 in 2010 (EAPC 0.7%, $p < 0.001$). Two thirds were astrocytoma, 10% oligodendroglioma/oligoastrocytoma, 3% ependymoma and 21% were unspecified. Within the group of astrocytic tumours, the proportion of glioblastoma rose, while the proportion of anaplastic and unspecified astrocytoma decreased. Unspecified neoplasms also decreased, but this was significant only after 2005. Over the course of the study period, glioblastoma patients more often received multimodality treatment with chemotherapy concomitant and adjuvant to radiotherapy. The crude two-year survival rate of glioblastoma patients improved significantly, from 5% in the time period 1989–1994 to 15% in 2006–2010, with median survival increasing from 5.5 to 9 months. The incidence of low-grade gliomas did not change over time. Survival rates for low-grade oligodendroglial and mixed tumours show a modest improvement.

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Conclusions: The incidence rate for the total group of gliomas slightly increased, with a decrease of anaplastic and unspecified tumours and an increase of glioblastoma. Following the introduction of combined chemoradiation, two-year survival rates for glioblastoma significantly improved. Survival improved for low-grade gliomas except for low-grade astrocytic tumours.

1. Introduction

Gliomas form a heterogeneous group of tumours of neuroepithelial tissue which comprise the majority of malignancies of the central nervous system (CNS) [1–3]. On the basis of their histopathology, gliomas are classified into astrocytoma, oligodendroglioma, oligoastrocytoma (or 'mixed' glioma) and ependymoma, and subdivided into grade I–IV according to the World Health Organisation (WHO) grading system [4]. Gliomas represent a relatively rare but serious health burden in terms of morbidity and mortality. Despite significant advances in diagnostics and therapeutics over the past decades, prognosis for patients with high-grade gliomas (WHO grade III and IV tumours) remains dismal, with disease generally recurring even after optimal initial treatment. For instance, addition of the alkylating agent temozolomide to the therapeutic arsenal against glioblastoma (WHO grade IV astrocytoma) increased median survival of patients by a mere 2.5 months [5], or 4.6 months in those having undergone complete resection [6].

Notwithstanding their more favourable characteristics, low-grade gliomas (WHO grade I and II tumours) may eventually cause a variety of neurological symptoms including epilepsy and cognitive disorders [7], and some have a marked potential for malignant progression. Unfortunately, complete surgical removal is commonly unfeasible due to diffuse brain infiltration [8], and procedures carry the risk of causing impairment themselves. Optimal treatment strategies have long been subject of debate [9,10]. While some advocate active surveillance until progression as a reasonable option [11,12], notably in (younger) patients who experience seizures as the only symptoms of disease [13,14], recent guidelines recommend a more active approach, with surgical tumour debulking as the preferred first course of action in most cases [15,16].

On several occasions, population-based surveys have reported rising incidence of brain tumours including gliomas in adults [17,18]. These trends should, in retrospect, be largely attributed to improved detection, in particular of low-grade tumours following introduction of computed tomography (CT) and magnetic resonance imaging (MRI) [19,20], and increased efforts to obtain histopathological diagnosis [21,22]. Indeed, the observed increase did not coincide with sudden increases in mortality rates [23]. Recent years show a stabilising or even declining incidence [2,24–26]. Some caution is warranted in interpreting these findings, however, since trends are sensitive not only to developments in diagnostic and therapeutic practices, but may also be impacted on by changes in histologic criteria and revisions in classification schemes [27,28].

The present report describes the incidence and survival of CNS gliomas in adults diagnosed in the Netherlands during the time period 1989–2010. In addition, we show survival patterns for the major histological groups of glioma, thereby focusing on glioblastoma and low-grade gliomas.

2. Materials and methods

2.1. Data sources

Electronic patient records were derived from the Netherlands Cancer Registry (NCR), which covers a nation with approximately 16.6 million inhabitants. Newly diagnosed cancer patients are notified to the registry by the Dutch Pathology Network (PALGA), to which pathology departments submit their reports on histological, cytological and autopsy examinations. Additional information on patient and tumour characteristics, diagnostics and therapy is collected from hospital records by trained registry personnel of the NCR. Topography and morphology are coded according to the International Classification of Diseases for Oncology (ICD-O). Additional cases as well as case ascertainment are provided by the national hospital discharge database. The NCR lacks information on patients who are seen only by outpatient departments, and this underregistration has previously been estimated to be less than 2% [29], with missing cases mostly being elderly patients with digestive tract tumours [30].

We obtained follow-up information on vital status for all cases through linkage with the Municipal Personal Records Database (GBA). No data were available on disease progression or recurrence. The study design, data abstraction process and storage protocols were approved by the national supervisory committee of the NCR.

2.2. Selection of cases

From the NCR, we selected adult patients ($\geqslant$18 years of age) with a glioma in the brain or spinal cord (topography codes C71.0–C72.9) diagnosed during