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Purpose. Understanding the presentation of spinal cord injury (SCI) due to tumours considering population distribution and temporal trends is key to managing SCI health services. This study quantified incidence rates, function scores, and trends of SCI due to tumour or metastasis over an 18-year time period in a defined region in Spain. Methods. A retrospective cohort study included in- and outpatients with nontraumatic SCI due to tumour or metastasis admitted to a metropolitan hospital in Spain between 1991 and 2008. Main outcome measures were crude and age- and sex-adjusted incidence rates, tumour location and type, distribution by spinal level, neurological level of injury, and impairment ASIA scores. Results. Primary tumour or metastasis accounted for 32.5% of nontraumatic SCI with an incidence rate of 4.1 per million population. Increasing rates with age and over time were observed. Major pathology groups were intradural-extramedullary masses from which meningiomas and neurinomas accounted for 40%. Lesions were mostly incomplete with predominant ASIA Grade D. Conclusions. Increasing incidence rates of tumour-related SCI over time in the middle-aged and the elderly suggest a growing need for neurooncology health resources in the future.

1. Introduction

Nontraumatic spinal cord injury (SCI) accounts for a significant proportion of all SCI unit and rehabilitation admissions [1, 2], and allocation resources should take into account incidence and trends over time. Although cases of traumatic origin account for the largest proportion of SCI, and most SCI studies have been conducted in this group, nontraumatic SCI recently has received more attention [3–7]. The diverse underlying pathologies of nontraumatic SCI translate into differences in case ascertainment time, clinical outcomes, case management, and functional expectations [3, 6, 8–10]. The principal causes of nontraumatic SCI are primary or metastatic tumours. Tumour, intradural or extradural lesions, can cause a wide spectrum of SCI symptoms by either spinal cord compression or invasion and destruction of the spinal cord or its vasculature. Advances in diagnosis and treatment lead to earlier and higher detection of cancer and central nervous system involvement as well as to increased survival rates [8]. Subsequently, neurooncology units will increasingly be confronted with frequent admissions of patients presenting SCI due to tumour or metastasis.

Although demographic observational reports on SCI due to tumour or metastasis have been published, there is a lack...
Table 1: Incidence and demographics of spinal cord injury due to primary tumour or metastasis in Aragón, Spain, 1991–2008. European population taken as standard for direct adjustment.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>SCI incidence</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of cases</td>
<td>32</td>
<td>58</td>
<td>90</td>
</tr>
<tr>
<td>Crude incidence rate</td>
<td>2.7</td>
<td>5.8</td>
<td>4.1</td>
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<tr>
<td>Adjusted incidence rate</td>
<td>2.5</td>
<td>4.8</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>2.2</td>
<td>4.2</td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>2.8</td>
<td>5.3</td>
<td></td>
</tr>
<tr>
<td>Sex, % male</td>
<td>43.8</td>
<td>43.1</td>
<td>43.3</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>52.1 (19.5)</td>
<td>60.1 (17.0)</td>
<td>57.3 (18.3)</td>
</tr>
<tr>
<td>Males</td>
<td>52.5 (19.6)</td>
<td>57.7 (19.6)</td>
<td>55.8 (19.5)</td>
</tr>
<tr>
<td>Females</td>
<td>51.8 (20.0)</td>
<td>62.0 (14.9)</td>
<td>58.4 (17.4)</td>
</tr>
</tbody>
</table>

of studies on incidence and trends over time. They are needed to manage allocation and delivery of health resources in population-based neurooncology settings. In order to address this goal, description of disease frequency taking into account population distribution and temporal trends is needed [9, 10].

This study aims to quantify incidence rates, functional scores, and trends of SCI due to tumour or metastatic origin in Aragón, a well-defined autonomous region in Spain over an 18-year period, and thereby seeks to anticipate for healthcare and rehabilitation resource needs in this group of patients. Specific research objectives addressed were the description of (1) incidence rates of SCI by age and sex, (2) causes of injury, and (3) severity and impairment level injury.

2. Methods

In Spain, patients are treated and followed up mainly in the region where they live due to the decentralization of health services. If an illness onset occurs outside the region, ultimately the patient is transferred back to the region of residence for follow-up. There are 13 specialized SCI units in the Spanish National Health System. Hospitals in the catchment area that take care of patients with SCI as secondary diagnosis, which is the case with tumoral SCI, send them to the Miguel Servet University Hospital at least for routine clinical data monitoring. That hospital is a 1200-bed public hospital in Northeastern Spain. The SCI unit of such centre is the only specialized SCI unit for up to two million inhabitants, the population of the administrative region of Aragón. Records from the SCI unit of all in- and outpatients with nontraumatic SCI due to tumour or metastasis between January 1991 and December 2008 were retrospectively reviewed. These records included referrals from other hospital units. Additionally, to capture cases not registered within the SCI unit, hospital archives and central databases from the hospital were examined using the CIE-9-MC classification.

Specification of SCI patient demographics, causes of damage, neurological level, and ASIA functional classification were extracted from the records. Additionally, age- and sex-specific population data for Aragón for each year from 1972 up to and including 2008 were obtained from the Statistics National Institute, maintained by the Government of Spain [11].

The data were divided into two time intervals, 1991–2000 and 2001–2008, to ease the observation of general trends over time. Incidence cases were grouped according to sex, age at the time of injury, and decade. Crude incidence rates were calculated within the range of 0–80 years using 10-year units and for each time interval. In addition, population denominators from the Statistics National Institute were used to construct annual age- and sex-specific incidence rates of SCI. The midyear population census for each year was used for aggregated data. Finally, in order to control for the effects of different population age distributions, crude incidence rates were age- and sex-adjusted to the European population to facilitate comparison with other studies. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the local health research ethics board of the Carlos III Health Institute, Madrid, Spain (2008/01).

3. Results

A total of 277 nontraumatic cases were identified during the 18-year period studied, from which 90 (32.5%) were due to primary tumour or metastasis as shown in Table 1. The most common primary cancer sites for metastasis were lymphoma, as well as breast, lung, and prostate. Just over half of the cases (56.6%) were women. Mean age at diagnosis for women was 52 years for the first period (1991–2000) and 62 years for the second period (2001–2008), that is, approximately raising a year per calendar year. For men it was 53 years for the first period (1991–2000) and 58 years for the second period (2001–2008), an increase 50% lower than for women.

The incidence rate adjusted by sex and age, covering the whole study period, was 4.1 per million population: 3.6 per million for men and 4.6 per million for women. Incidence rates in the second period (2001–2008) almost doubled with respect to the first period (1991–2000); see Table 1. Although generally incidence increased with age, patterns were different for men and women. In the second
period (2001–2008), for men, the strong increase in incidence was observed over 50 years of age, but for women this increase occurred ten years earlier at the age of 40 (Figure 1). The increase in cases from the first (1991–2000) to the second period (2001–2008) was higher among women.

According to their location, most tumours and metastasis were located intradural-extramedullary (Figure 2(a)), including meningiomas (26%) and neurinomas (14%) (Figure 2(b)). Extradural metastasis (mostly from carcinomas of the breast and prostate and from lymphoma) and intramedullary gliomas accounted each for 15.6% of the cases. Angiomas were distributed intramedullary and accounted for 6.7% of all cases. The increase between periods for women was remarkable for meningiomas (360% increase) and neurinomas (260% increase). There has been a reduction of gliomas and angiomas over time although overall number of cases has been small (14 and 6, resp.).

Location of damage was variable across spinal cord levels. Frequency distribution in Figure 3 shows that injury mainly occurred at the thoracic segments (56.7%), with frequency peaks at T4 and T12. Cervical lesions accounted for 17.8% of the cases and lumbar and sacral lesions for 14.4% and 11.1%
of the cases, respectively. In 10% of the cases the location was unknown. As seen in Figure 4, lesion location varied according to the histopathology of the tumour or metastasis. Epidural tumours, mainly metastasis, were situated mostly at thoracic and lumbar levels and meningiomas at thoracic level. Intramedullary gliomas were found at cervical, low-thoracic, and lumbar levels. Other tumours were distributed over the full length of the spinal cord.

Functional ASIA score was recorded in 73% of the cases with most missing data in the first period (1991–2000). Distribution of scores for incomplete lesions followed a shifted bell-shaped curve with highest numbers in Grade D (47%) as seen in Figure 5. Complete lesions (ASIA Grade A) were found in 13.6% of the patients.

### 4. Discussion

In the present study, we describe incidence, neurological function, and time trends of SCI due to tumour or metastasis in Aragon, Spain. From the first (1991–2000) to the second (2001–2008) studied time period, incidence rates more than doubled. Additionally, incidence rates increased with age in both males and females. The results suggest that the increase in females is mainly due to higher numbers of meningiomas and neurinomas. Neurological function was
not greatly affected, possibly since most cases presented with incomplete lesions in both time periods.

The comparability of incidence rates of tumoural SCI in Spain with other countries in and outside Europe is problematic due to lack of such information in the literature. Reports commonly are retrospective case-series from medical centres or case reports describing number of cases and studied period, but typically not catchment area or with lack of demographical data. Therefore, medical articles mainly reporting clinical data omit a potential epidemiological perspective [12–15], hence making a limited contribution to the implementation of health services for individuals with SCI due to tumour or metastasis. This population-based study, covering an 18-year time period, is novel showing age- and sex-adjusted incidence rates and trends of tumoural SCI.

Proportions of primary and secondary tumours differ from previous reported results: McKinley et al. [1] showed that 85% of the lesions were due to metastatic tumours and in an Italian recent report [15] this was 24%, compared to 16% in the present study. Possibly these differences can be explained by the above-mentioned discrepancy in data reporting. One additional explanation may well be the increased awareness among physicians of the devastating effects of SCI in cancer patients. This has resulted in more frequent use of palliative radiation therapy and bisphosphonates in those with spinal metastases leading to reduced SCI involvement.

Previous reports [14, 15] have observed that in individuals with tumoural SCI a higher proportion of lesions affect the thoracic levels, which is consistent with our study results. However, one should bear in mind that anatomically there are more thoracic metameric levels than lumbosacral or cervical ones. The data revealed that the site of lesion varied according to the cause. In the present study, metastasis and meningiomas accounted for most cases. In Spain it is known that the most frequent tumours are those due to lung cancer in men and breast cancer in women and that incidence rates of the later have increased over the last decades [16]. However, we have seen that rates of spinal cord metastases including those of breast cancer have not changed much over the studied time periods. Rates that did raise over time, mainly observed in women, were due to meningiomas, involving primarily thoracic levels, and neurinomas. Although the study period covered 18 years, the amount of data is too little to draw firm conclusions about a univocal relationship between tumour type, metastasis and meningiomas accounted for most cases. In Spain it is known that the most frequent tumours are those due to lung cancer in men and breast cancer in women and that incidence rates of the later have increased over the last decades [16]. However, we have seen that rates of spinal cord metastases including those of breast cancer have not changed much over the studied time periods. Rates that did raise over time, mainly observed in women, were due to meningiomas, involving primarily thoracic levels, and neurinomas. Although the study period covered 18 years, the amount of data is too little to draw firm conclusions about a univocal relationship between tumour type, metastasis and meningiomas accounted for most cases.
the diagnosis is often delayed, for example, in patients who have back pain [30] or present with weakness [31]. However, advances in diagnosis lead to improved detection and identification of SCI cases caused by tumours and metastasis. This, together with a recently developed international SCI data set for nontraumatic SCI [5], hopefully will contribute to the increasing quality of future studies assessing incidence rates and epidemiological trends.

5. Conclusions

Patterns of age-specific incidence rates, such those found in the present study, reveal the age groups to which special disability healthcare efforts should be directed. Our study shows that risks increase with age and that tumoural SCI is mainly observed in the middle- and old-aged. This, as well as the high mortality rates of individuals with SCI that still exceed those of the age-matched nondisabled population, pleads for a focus on short term disability healthcare goals. Additionally, it emphasizes the need for a multidisciplinary approach and a quick evaluation process regarding patient transfer to nursing home, hospice, or home. Ultimately, this work allows for the conduct of future studies focused on health outcomes such as survival and quality of life for each subtype of tumoural SCI.

Abbreviations

SCI: Spinal cord injury.

Disclosure

The funders had no role in the study design; collection, analysis, and interpretation of the data; writing of the report; or the decision to submit the article for publication.

Conflicts of Interest

The authors have no conflicts of interest.

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