Neuroendocrine tumors of bronchus and lung in Europe: trends of incidence and survival

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Rationale for the study

Neuroendocrine tumors (NETs) are malignant tumors composed of the neuroendocrine cells and originating all over the body. Most frequently these tumors are found in the gastrointestinal tract and the bronchopulmonary system, reflecting the density of neuroendocrine cells in these tissues. In 2000, the World Health Organization (WHO) redefined the classification into a histological classification taking into account the differentiation of the tumor. Subsequently, this classification was adapted by the International Classification of Diseases for Oncology and included in the 3rd Edition (ICD-O-3). For NETs of the lung, the histological classification has not changed since 2000. These tumors are divided in typical and atypical carcinoids, and high-grade neuroendocrine tumors (carcinomas) which are classified as either large cell or small cell.

The prognosis of NETs is overall favorable, and an ongoing improvement of the survival has been reported (1,4). However survival improvement change according to the histotype (2) and overall limited information on survival improvement for NET of bronchus and lung are available.

Increasing incidence of NETs has been observed from the '80s in USA (1) and in some European countries: Denmark (3), Norway (4), and The Netherlands (2). This increase seems to be due to the widespread availability and reliability of immunohistochemical techniques in the last three decades which have allowed researchers to identify cells with common neuroendocrine markers in virtually every organ. However, despite the increase in the number of published papers focused on NET, we still lack adequate epidemiological data for Europe overall and many EU country/regions. Cancer statistics are usually available only for broad categories not including the histotype so important for an appropriate description of the NET epidemiology. CI5CIX provide information on histotype but it includes only the small cell histotype of NET among lung tumors.

With this background it is important to study the epidemiology of NET in Europe focusing on all the histotype and on how their incidence and survival changed over time. Considering that NET survival is different per histotype, the incidence analyses by histotype will contribute to interpret the survival trend.

Aim of the study

To describe the epidemiology of NET of bronchus and lung in Europe and how incidence and survival changed in the period 1990-2007.

Methods of the proposed analysis

We will focus on NET of bronchus and lung C34.0-34.9. Morphology are listed in the table below.

	ICD-O3 morphology code
Typical carcinoids	8240/3-8245/3; (8248/1 if available)
Atypical carcinoids	8249/3
Small cell endocrine carcinoma	8041/3-8045/3
Large cell endocrine carcinoma	8013/3, 8246/3

Relative survival (cohort approach)

Five year relative survival will be estimated with the Hederer II method for the period of diagnosis 2000-2004. Pooled survival estimates for Europe will be derived as weighted averages of the region-specific

estimates, with weights reflecting the proportionate population in the regions. Five year relative survival will be provided by age, sex and histotype.

Survival time trend

Relative survival time trend for cancer patients diagnosed from 1990 to 2004 for Europe overall. We will select CR on the basis of the period and follow-up available in the CR in order to ensure the inclusion of the highest number of CR. A cohort approach will be used and accordingly the study period will be divided in 3-years intervals. Modelling will be used to test the significance of differences by sex, age class, histotype, geographic regions and to assess whether the observed increases in survival over the study period were real or randon (5). Survival trends will be provided by histotype. It could be useful to verify the availability of the information on the extend of disease for NET lung. In case, CR with at least the 75% of information available will be selected to study this important prognostic factor.

Incidence

Crude incidence rates per 100,000 with 95% confidence intervals will be estimated for sex, age-group and NET histotype for the period of diagnosis 2000-2007.

Incidence time trend

Joint Point method will be used for incidence time trend analysis for the period 1990-2007. CR will be selected on the basis of data available for the period of the study. Incidence time trend will be analysed for NET and for each histotype in Europe.

EUROCARE data items requested
Date of birth
Date of diagnosis
Date of death
Vital Status
Sex
Multiple tumour code
ICD-O3 morphology
Extend of disease (if available)
Life table
Population data

Proposed time schedule for the study
It is very important for us to have preliminary analyses available for summer. Dr Giuseppe Pelosi is involved in the revision of the classification of NET for bronchus and lung and it would be essential to include in such revision European data. The discussion on the revision of the classification will start in June.

Bibliography

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