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Original Research

Unknown primary carcinoma in the Netherlands: decrease in incidence and survival times remain poor between 2000 and 2012



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KEYWORDS

Unknown primary carcinoma; Population-based; Incidence; Survival; Cancer registry; Oncology **Abstract** *Backgroundlaim:* Unknown primary tumour (UPT) is the term applied to metastatic cancer, the origin of which remains unidentified. Since cancer treatment is primarily based on the tumour site of origin, treatment of UPT patients is challenging. The number of reports on incidence, treatment and survival of UPT is limited. We hereby report data on patients (2000–2012) with UPT in the Netherlands.

Methods: The age-standardised rate (ASR) of 'other and unspecified' malignancies in the Netherlands was compared with other European countries. Patients diagnosed with UPT between 2000 and 2012 were selected from the Netherlands Cancer Registry (NCR) to calculate incidence rates. Patient characteristics, treatment and survival rates were assessed.

Results: The ASR of 'other and unspecified' malignancies in the Netherlands did not differ from the European average ASRs (2008–2012). A total of 29,784 patients with an unknown primary tumour were selected from the NCR (2000–2012). The incidence decreased from 14 per 100,000 person years (European standardised rate) in 2000 to 7.0 in 2012. The most common metastatic sites were liver, lymph nodes, bone and lung (42%, 22%, 16% and 14%, respectively), and approximately two-thirds of patients were diagnosed with metastases at a single site. One-third of the patients were treated; these were mainly younger patients. The overall

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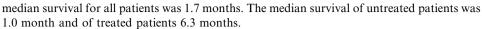
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Conclusion: The incidence of UPT between 2000 and 2012 is decreasing in the Netherlands, and one-third of these patients received treatment. Survival after diagnosis is limited to months rather than years.

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1. Introduction

Unknown primary tumour (UPT) represents a heterogeneous group of metastasised malignancies, the origin of which is not detected during a patient's lifetime. If it cannot be verified if all the guideline recommendations regarding intensive diagnostic workup were met, the malignancy is instead described as carcinoma of unknown primary (CUP). The most common sites of metastatic disease are liver, lymph nodes, lungs and bones [1-3]. Worldwide, the reported incidence is estimated to be around 3-5% of all newly diagnosed cancers, which is an overall age-standardised incidence of between 4 and 19 cases per 100,000 person years [4,5]. However, the exact incidence is difficult to determine since only a limited number of countries report on the incidence of CUP [6-11]. In addition, guidelines on CUP and techniques for its diagnostic workup differ internationally, as do cancer registry regulations on when a patient may be registered as having CUP.

In general, treatment of malignancies is based on the site of origin as this is more effective than empirical treatment with radiotherapy and/or chemotherapy [5,12–14]. Consequently, most guidelines on CUP focus less on treatment and more on diagnostic strategy. Diagnostic strategy comprises an initial general diagnostic approach followed by a second diagnostic approach based on the results of the first. This approach focuses on the suspected primary tumour site. Compared with patients with a known primary tumour, patients with UPT face a longer diagnostic workup with additional diagnostic procedures, which are not always risk-free and might negatively influence quality of life. The median survival of patients diagnosed with a malignancy of unknown primary origin is reported to be around 3-10 months [15-22].

The number of reports of UPT is limited. In this article, we report on the incidence, treatment and survival of UPT patients in the Netherlands diagnosed between 2000 and 2012.

2. Materials and methods

2.1. Data source

The age-standardised rate (ASR) of 'other and unspecified' malignancies in the Netherlands was compared

with other European countries, using the data published in 'Cancer Incidence in Five continents Vol. XI' by International Agency for Research on Cancer (IARC). Data were extracted from the separate incidence tables of the countries and compared.

The nationwide population-based Netherlands Cancer Registry (NCR) registers all newly diagnosed malignancies. PALGA, the Dutch pathology reporting system automatically sends out reports, and independently and uniformly trained NCR data managers collect data from original patient files. Non-histologically verified tumours are entered into the cancer register by linking with the Dutch National Registry of Hospital Discharge Diagnosis, which is a near-complete registry of hospital discharge data on all in-hospital treatment. Information on patient characteristics, tumour characteristics, treatment, hospital of diagnosis, hospital of treatment and vital status is recorded. The International Classification of Diseases for Oncology (ICD-O) is used for coding tumour site and morphology [23]. The vital status of all patients is actively obtained on a regular basis through linkage of the cancer registry data with the database of the Personal Records Database (BRP). Municipalities keep personal details, such as name, gender, births, marriages and deaths, in the BRP of residents of the Netherlands and of persons who have left the Netherlands (nonresidents).

2.2. Outcomes and statistical methods

The UPTs were selected from NCR data from 2000 to 2012. The ICD-O code 'C80' was used if the primary tumour site was unknown, and no suspected site of origin was mentioned in the patient files. Benign tumours, tumours with a suspected primary tumour site and recurrent malignancies were excluded. All metastatic sites are now registered in the NCR, but these were not documented in all regions of the Netherlands until 2010. For analyses involving metastatic sites, only those patients for whom the site of metastasis was registered were included. Furthermore, multiple metastases of the same type were counted as one, e.g. bone metastases in hip and vertebra were counted as one metastatic site. Additionally, we chose to report each of the metastatic sites which resulted in a total number of metastatic locations that exceeded the total number of patients since one patient can have multiple metastatic sites. The vital status of patients was assessed on 1

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