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Trends in incidence, initial treatment and survival of myelodysplastic syndromes: A population-based study of 5144 patients diagnosed in the Netherlands from 2001 to 2010

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Abstract ***Background:*** Studies with long-term follow-up of patients with myelodysplastic syndromes (MDS) based on data from nationwide population-based cancer registries are lacking. We conducted a nationwide population-based study to assess trends in incidence, initial treatment and survival in MDS patients diagnosed in the Netherlands from 2001 to 2010.
Methods: We identified 5144 MDS patients (median age, 74 years) from the Netherlands Cancer Registry (NCR). The NCR only includes MDS cases that were confirmed by bone marrow examinations. Information regarding initial treatment decisions was available in the NCR.
Results: The age-standardised incidence rate of MDS was 2.3/100,000 in 2001–2005 and 2.8/100,000 in 2006–2010. The incidence increased with older age, with the highest incidence among those aged ⩾80 years (32.1/100,000 in 2006–2010). Forty-nine percent of all MDS cases were unspecified. Of all patients, 89% receive no treatment or only supportive care and 8% were started on intensive therapy as initial treatment. Survival did not improve over time. The 5-year relative survival was 53%, 58%, 48%, 38% and 18% in patients with refractory anaemia (RA), RA with ringed sideroblasts, 5q-syndrome, refractory cytopenia with multilineage dysplasia, and RA with excess blasts, respectively.
Conclusion: The incidence of MDS increased over time due to improved notification and better disease awareness, and has stabilised since 2007. The classification of MDS seems challenging as

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almost half of the pathologically confirmed cases were unspecified. The lack of improvement in survival might be explained by the limited availability of therapeutic agents. Therefore, ameliorated management and new treatment options are warranted.

1. Introduction

The myelodysplastic syndromes (MDS) constitute a heterogeneous group of clonal haematopoietic stem cell disorders characterised by ineffective hematopoiesis and an increased risk of leukaemic transformation [1]. At the beginning of the new millennium, the World Health Organization (WHO) classified MDS as malignant myeloid neoplasms [2,3], and consequently MDS became reportable malignancies to population-based cancer registries as of 2001. The age-standardised incidence rate (ASR) of MDS is currently 2.0 to 3.4 per 100,000 in Western countries and the incidence increases sharply with older age [4–8]. Life expectancy of patients with MDS is variable and is dependent on the MDS subtype, and several clinical and prognostic parameters [9–13]. Treatment decisions also rely on clinical and prognostic parameters [14–16].

Recent clinical studies have reported favourable outcomes in patients with MDS after treatment with immunomodulatory agents (e.g. lenalidomide [17] or hypomethylating agents (i.e. azacitidine [18] and decitabine [19]. Survival data derived from clinical trials can be biased, however, because of patient selection (e.g. exclusion of elderly patients with comorbidities) [20]; therefore, inference about the general patient population might not be made. The availability of nationwide population-based studies with long-term follow-up on incidence and survival in an unselected MDS population are lacking. In the few reported population-based studies on incidence and survival in MDS, the period of patient inclusion was short and the follow-up period was limited [4–6,21]. Furthermore, population-based studies regarding treatment decision in the entire MDS population have not been reported previously.

We have performed a nationwide population-based study in more than 5000 newly diagnosed patients with MDS in the Netherlands from 2001 to 2010 reported to the Netherlands Cancer Registry (NCR). The aim of this study was to assess trends in incidence, initial treatment and survival among these MDS patients.

2. Patients and methods

2.1. The Netherlands Cancer Registry

Established in 1989, the population-based nationwide NCR is maintained and hosted by the Comprehensive Cancer Centres. The NCR is based on notifications of all newly diagnosed malignancies in the Netherlands by the automated nationwide archive of histopathology and cytopathology (PALGA), to which all pathological laboratories report. The NCR also receive notifications from the national registry of hospital discharges and various haematology departments. Information on date of birth, sex, date of diagnosis, morphology, and initial treatment decision is routinely collected by trained registrars from the medical records. The registrars register the diagnosis that is given by the treating physician. Initial treatment is recorded in four categories by the NCR, namely no therapy or only supportive care, chemotherapy, chemotherapy followed by a stem cell transplantation (SCT), and other therapy.

2.2. Diagnostic criteria and study population

MDS was included in the NCR as of 1st January 2001 when the International Classification of Diseases for Oncology Third Edition (ICD-O-3) was implemented for case ascertainment [2]. Notification of MDS is possibly incomplete in the first years after implementation of the ICD-O-3 seeing that implementation of the new WHO classification into clinical practice and notification sources of the NCR will have been delayed. Cases of MDS classified as non-malignant after 2000 will not have been notified to the NCR.

The NCR exclusively includes MDS cases that were confirmed by bone marrow examinations. All MDS subtypes according to the ICD-O-3 morphology codes are included in the NCR, namely refractory anaemia (RA; 9980), RA with ringed sideroblasts (RARS; 9982), RA with excess blasts (RAEB; 9983), refractory cytopenia with multilineage dysplasia (RCMD; 9985), MDS with isolated deletion 5q (5q-syndrome; 9986) and MDS not otherwise specified (MDS NOS; 9989). The ICD-O-3 is developed by the WHO and is in accordance with the disease definitions according to the third edition of the WHO classification of haematological malignancies [3].

All patients diagnosed with MDS between 2001 and 2010 were identified from the NCR. Patients were observed from date of diagnosis to date of death, date of emigration or end of follow-up (i.e. 1st February 2012). Death dates were retrieved from the nationwide population registries network, which holds vital statistics of all Dutch residents.

2.3. Statistical analysis

ASRs of MDS were calculated per 100,000 person-years for the entire study period (2001–2010), two