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Trends of incidence, mortality, and survival of multiple myeloma in Switzerland between 1994 and 2013

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ABSTRACT

Background: Treatment of multiple myeloma has changed considerably over the last two decades with remarkable reduction in mortality rates in clinical trials and in population-based studies. Since health care systems and patient management differ between countries, population-based data from cancer registries with high coverage may provide further insight into real-life achievements and unmet needs. We report on the first population-based nation-wide study of incidence, mortality and survival of multiple myeloma in Switzerland covering the era of autologous stem cell transplantation and the first proteasome inhibitors and immunomodulatory drugs.

Methods: We performed a retrospective registry study with data from the National Institute for Cancer Epidemiology and Registration (NICER) database in Switzerland from 1994 to 2013.

Results: We identified 5770 patients with multiple myeloma. Incidence has increased from 419 new cases per year in 1994–1998 to 557 new cases per year in 2009–2013 while the age-adjusted incidence rate remained stable at 4.7–5.0 per 100'000 person-years. Five- and 10-year relative survival increased from 32.6% (95%CI 29.3–36.0) and 17.8% (95%CI 14.9–21.0) in 1994–1998 to 46.4% (95%CI 43.3–49.3) and 25.0% (95%CI 21.9–28.3) in 2009–2013.

Conclusion: The increase in incidence can be attributed to demographic changes. There is a trend to longer relative survival in all age groups with substantial increase in myeloma patients aged less than 75 years and only minimal changes in older persons.

1. Introduction

Multiple myeloma is one of the most frequent haematological malignancies. During the last 20 years advances in treatment had a marked impact on survival of patients with myeloma. Since the introduction of melphalan for myeloma treatment in the 1960s [1], no treatment has shown further improvement in survival rates until the 1990s [2]. Thereafter, high-dose chemotherapy combined with autologous stem cell transplantation [3–6] and new drugs, including thalidomide [7–9], bortezomib [10,11] and lenalidomide [12–14] have been introduced and significant survival advantages of these therapies compared to former standard treatment have been demonstrated in randomised controlled trials. Furthermore, bisphosphonates [15–17] have shown anti-myeloma activity and a survival benefit in myeloma patients. In addition, general improvements in supportive care, for instance, better transfusion support and anti-infective treatment, may have improved outcome even if there were no specific prospective trials for survival outcome in myeloma patients.

Since experimental prospective clinical trials are confined to selected myeloma patients, their results are not readily transferable to the real-life setting. In recent years, several population-based epidemiological studies have shown significant improvements in survival for myeloma patients in different countries [18–21]. Nevertheless, access to treatment, health care systems, demographic patterns and patient management differ between regions and may have an impact on incidence and mortality rates. Therefore, we think it is important to complement experimental trials and observational studies from selected patient groups with population-based nation-wide epidemiological data

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from different countries.

We performed a retrospective observational study with population-based cancer registry data from Switzerland in the era of high-dose chemotherapy with autologous stem cell transplantation and the first proteasome inhibitors and immunomodulatory drugs before newer treatments such as antibody-therapies or second generation proteasome inhibitors have become widely available. Objectives were analysis of trends in incidence, mortality and survival in the light of these treatment advances.

2. Methods

2.1. Data sources and inclusion criteria

Incident multiple myeloma cases of the years 1994–2013 and corresponding vital status information were obtained from the National Institute for Cancer Epidemiology and Registration (NICER) database. NICER is collecting and harmonizing cantonal cancer registry (CR) data and provides a central national database of cancer registration data in Switzerland. The earliest CR data is available from Geneva dating back to 1970, followed by Vaud and Neuchâtel (1974), Zurich (1980), St. Gallen-Appenzell (1980), Basel-Stadt and Basel-Landschaft (1981), Valais and Graubünden (1989), Glarus (1992), Ticino (1996), Jura (2005) and Fribourg (2006). More recently, cancer registration has been introduced in Lucerne (2010), Nidwalden, Obwalden, Uri, Zug (2011), Thurgau (2012) and Aargau (2013). Due to the gradual introduction of cancer registration, national population coverage for this study varied from 56.1% (1994–1998) to 67.0% (2009–2013).

Mortality data, mid-year population estimates and cantonal death rates by age, sex and calendar year were supplied by the Swiss Federal Statistical Office (SFSO), referring to all persons with permanent residence status in Switzerland. The mortality information is based on SFSO standardized death certificates. The coding of death certificates and the selection of the underlying cause of death is carried out by the SFSO for the whole of Switzerland. Up to 1994, causes of death were coded according to the eighth revision of the International Classification of Diseases and Related Health Problems (ICD-8). Since 1995 the coding system of the tenth revision (ICD-10) has been used.

Incidence analyses were based on all reported cases with primary multiple myeloma, diagnosed in the time period 1994–2013. Survival analyses were restricted to cases of CRs providing vital status information to the pooled database, which led to the exclusion of cases from the canton of Vaud.

2.2. Analytic methods

We calculated five-year age-specific, crude and age-standardized incidence and mortality rates with corresponding 95% confidence intervals (95%CI) for subsequent five-year periods between 1994 and 2013. Age-standardized rates were calculated using the direct method and the European standard population [22] as reference population. For the estimation of the mean annual case frequencies of incident multiple myeloma cases, expected multiple myeloma cases from cantons without CR were added to the observed multiple myeloma cases from cantons covered by cancer registration. The expected number of multiple myeloma cases were estimated by applying the observed age- and period-specific incidence rates to the population of the cantons without cancer registration.

Relative survival (RS) was estimated by dividing the observed survival after diagnosis by the survival as expected in the general population of corresponding sex, age and calendar year. Observed survival (OS) was estimated based on transformation of the cumulative hazards. Expected survival was estimated using the Ederer II method [23] applied to smoothed sex-, age and calendar year-specific death rates of the Swiss population covered by cancer registration. We calculated OS and RS up to 10-years after diagnosis using period analysis for the time period 2009–2013 and conventional cohort analysis for the prior periods [23].

Statistical analyses were performed using Stata/MP version 13.1 (STAT Corp., TX USA).

Table 1
Patient characteristics of multiple myeloma cases reported to Swiss cancer registries, 1994–2013.

	N	%	Median age
Overall	5770	100.0%	71 years
Sex			
Males	3059	53.0%	70 years
Females	2711	47.0%	73 years
Age			
< 65 years	1746	30.3%	–
65–74 years	1723	29.9%	–
> 75 years	2301	39.9%	–
Time period			
1994–1998	1174	20.3%	72 years
1999–2003	1306	22.6%	72 years
2004–2008	1481	25.7%	71 years
2009–2013	1809	31.4%	71 years

Population covered by cancer registration: 56.1% in 1994–1998, 57.8% in 1999–2003, 60.9% in 2004–2008, and 67.0% in 2009–2013.

3. Results

Table 1 shows the demographic characteristics of observed multiple myeloma cases diagnosed between 1994 and 2013 in Switzerland. The median age at diagnosis was 70 years in males and 73 years in females and remained stable throughout the observed time period. Around 30% of all patients were younger than 65 years at the time of diagnosis, 28.6% in 1994–1998 and 31.0% in 2009–2013. The proportion of patients aged 85 and older stayed stable with around 9% across all time periods (data no shown). We estimated mean annual case frequencies of 419 and 557 incident multiple myeloma cases and 291 and 298 multiple myeloma deaths for the time periods 1994–1998 and 2008–2013, respectively (Table 2). The corresponding rates by five-year age groups are presented in Fig. 1. In both sexes, age-adjusted incidence rates stayed fairly stable over time (Fig. 2). For multiple myeloma mortality, we observed a continuous decline in age-standardized rates of both sexes (−12.1% in males and −27.5% in females) (Fig. 2), driven by the decline (−23.1%) observed in the population aged 65–74 years. Irrespective of time period, crude and age-standardized incidence and mortality rates were distinctly higher in males than in females. In 2009–2013, for example, the age-standardized incidence rates were 6.1 (95%CI 5.7–6.5) per 100,000 person-years (PYs) in males and 4.0 (95%CI 3.7–4.3) per 100,000 PYs in females. For the same time period, the following age-standardized mortality rates have been observed: 3.2 (95%CI 3.0–3.5) per 100,000 PYs in males and 2.0 (95%CI 1.9–2.1) (females) per 100,000 PYs in females.

Five- and 10-year RS increased from 32.6% (95%CI 29.3–36.0) and 17.8 (95%CI 14.9–21.0) in 1994–1998 to 46.4% (95%CI 43.4–49.4) and 25.0 (95%CI 21.9–28.3) in 2009–2013. The survival curves revealed an age-gradient with better OS and RS in younger patients (Fig. 3). In patients diagnosed below age 65 years, 5-year RS improved from 44.5% (95%CI 38.3–50.6) in 1994–1998 to 66.5% (95% 61.4–71.0) in 2009–2013 (Fig. 4). In patients diagnosed between age 65–74 years and above (75+ years), 5-year RS increased from 33.9 (95%CI 28.1–39.9) to 50.1% (95%CI 44.6–55.4) and 22.0 (95%CI 17.1–27.6) to 26.6% (95%CI 22.1–31.4), respectively. Ten years after diagnosis, only patients diagnosed before age 65 years showed substantial improvements in RS with 26.7% (95%CI 21.2–32.6) in 1994–1998 and 43.7% (95%CI 37.8–49.6) in 2009–2013 (Fig. 3).