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Testicular cancer: Trends in mortality are well explained by changes in treatment and survival in the southern Netherlands since 1970

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ABSTRACT

The aim of this study was to interpret changes in mortality from testicular cancer (TC) against the background of changes in treatment and survival in the south of The Netherlands.

Five-year moving average standardised mortality rates were calculated. Primary treatment and relative survival were analysed according to histology, stage and year of diagnosis.

The mortality rate dropped in the period 1979–1986 and then flattened out. The types of treatment that patients received did not change significantly over time and were according to the guidelines. Ten-year relative survival for seminoma TC patients improved from 81% (67–91%) in 1970–1979 to 95% (88–100%) in 2000–2002; for non-seminoma TC patients these rates were 54% (38–68%) and 92% (85–99%), respectively. Conditional 5-year relative survival for seminoma and non-seminoma TC patients 5 years after diagnosis was 99% and 96%, respectively.

In conclusion, there was an enormous increase in relative survival and a significant decrease in mortality.

1. Introduction

Although testicular cancer (TC) only accounts for 0.8% of all male cancers,[1] it is the most common malignancy amongst men aged 15–44 in developed countries. Of all TCs, 95% are germ cell tumours, which are grouped histologically into seminomas and non-seminomas.[2] The majority of the seminoma TCs are diagnosed amongst men in the age group of 30–45 years, while most of the non-seminoma TC patients are between the ages of 20 and 35 years.[2]

The incidence of TC is increasing throughout Europe, but there are large variations in the incidence rates and in the speed at which incidence increases across the European countries.[3] Relative survival of TC has increased during the last 40 years to an average 5-year rate of 93% in Europe,[4–7] but also with substantial variations across Europe.[6] In addition to stage at diagnosis,[8] age at diagnosis matters, younger

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patients exhibiting better survival than older patients.[8,9] Most of the increase in survival is primarily attributed to the introduction of effective cisplatin-containing chemotherapy for advanced disease in the 1970s.[4,10] Mortality has dropped by about 70% in the USA and Europe since the 1970s, but at a lower pace in Eastern Europe than in the European Union and the USA.[11]

The aim of this study was to detect trends in treatment, survival and mortality of TC in the south of the Netherlands from 1970 to 2004, where the management of TC was decentralised.

2. Patients and methods

2.1. Patients

The Eindhoven Cancer Registry (ECR) has collected data on all patients with newly diagnosed cancer in the southern part of the Netherlands since 1955.[12] Until 1988, only patients diagnosed in the eastern part of the area were registered, but since that year patients diagnosed in the middle and western part of North Brabant are also included. Nowadays, the registry serves a population of 2.4 million inhabitants. The area offers good access to specialised medical care in nine general hospitals and two large radiotherapy institutes. Information on diagnosis, staging and treatment was extracted from the medical records by trained registrars.

All testis cancer patients diagnosed between 1970 and 2004 were included in the study. The tumours are grouped according to histological origin, as described in the third revision of the International Classification of Diseases for Oncology (ICD-O)[13]: seminomas (ICD-O codes: 9060–9064), non-seminomas (ICD-O codes: 9065–9085, 9100–1902, 9105) or other. The stage grouping of the TNM-classifications of TC has changed over time in such a way that it became impossible to compare the different stage groups over time. We have therefore chosen to categorise the extent of the disease as: localised (any T, N = 0 and M = 0), lymph node metastasis (any T, N > 0 and M = 0), distant metastasis (any T, any N and M > 0) and unknown. Patients with stage unknown were left out of the stage-specific analysis. Stage was recorded reliably from 1980 onwards, so only patients diagnosed since then were included in the stage-specific analyses.

2.2. Treatment

Five major subgroups were considered for primary treatment: surgery only, surgery and radiotherapy, surgery and systemic therapy, unknown and other/none. The specific type of therapy was not registered, therefore it was not possible to identify whether a patient received cisplatin-containing chemotherapy or another type of chemotherapy.

A fisher-exact test was used to test whether there was an overall change in administered treatment over time. This was done according to histology and stage.

2.3. Relative survival

Data on vital status (available until 1st January 2005) were obtained from the hospital records and the mortality register of the Central Bureau for Genealogy (an institution that registers all deaths in the Netherlands via the municipal population registries). Data on vital status were only available for patients diagnosed in or before 2002.

Relative survival is an estimation of the disease-specific survival. It is calculated as the absolute survival amongst cancer patients divided by the expected survival for the general population with the same sex and age structure.[14] Relative survival was computed with the traditional cohort-analysis for periods with complete 5 and 10-year follow-up. Period analysis was used to estimate the relative survival for the most recent periods with incomplete 5 or 10-year follow-up.[15] Survival analyses were carried out according to histology and stage.

Conditional survival was computed with period analysis for patients diagnosed between 1970 and 2002, and was performed according to histology. Five-year relative survival was computed for every additional year survived, conditional on being alive at that moment. Since patients who have already survived for some years are older than at diagnosis, conditional relative survival rates were also adjusted for survival in the general population with the same age distribution as patients at that time. A conditional 5-year relative survival at year x is the 5-year relative survival for patients who are still alive x years after diagnosis of TC.

2.4. Mortality

Mortality data were obtained from Statistics Netherlands for the period 1970–2005. Five-year moving average European standardised mortality rates per 100,000 person–years were calculated and compared to the Dutch testicular cancer mortality.[16] In addition, trend estimated annual percentage of change analysis was performed for different time periods. For the period 1970–1988 the Dutch mortality rates were only available as crude mortality rates.

3. Results

3.1. Treatment

In total, 966 patients were included for treatment analysis (54% seminoma and 46% non-seminoma).

The overall treatment of the localised seminoma TC patients changed significantly ($p < 0.0001$) over time (Fig. 1a), the surgery alone treatment was lower in the period 1990–1999 than in the other two periods. While the percentage of patients who received surgery and radiotherapy was higher in the period 1990–1999 (93%) in contrast to the periods 1980–1989 (82%) and 2000–2004 (85%). The treatment in the group of seminoma TC patients with lymph node metastasis changed significantly ($p < 0.001$), the percentage of patients who received surgery and radiotherapy decreased from 58% in the 1980s to 32% in the period 2000–2004, while the percentage of patients who received surgery and systemic therapy increased from 33% to 64% in the same period. The distant metastases seminoma TC patients exhibited no significant differences in treatment over time, the number of patients in this group was small ($n = 22$).

In the non-seminoma treatment group there was a significant difference ($p < 0.0001$) in the treatment of patients with