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Original Paper

Hodgkin's Disease in a National and Hospital Population: Trends Over 20 Years

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The aim of the study was to investigate the incidence rate and time trends in a national registry population of Hodgkin's disease (HD) and the effects of selection in a hospital population. A national registry population of all HD patients from Norway and a hospital population of HD patients treated at the Norwegian Radium Hospital (NRH) were studied retrospectively from 1971 to 1993. The incidence of non-Hodgkin's lymphomas (NHL) in Norway increased steadily from 1961 in contrast to a stable incidence pattern for HD before 1980 and a decreasing incidence since 1980. Due to improved diagnostic tools after 1980, an increasing proportion of patients previously diagnosed as lymphocyte depleted and unclassified HD were classified as NHL. As these histologies are dominant in older patients, the incidence of older patients with HD and the total population of HD have decreased since 1980. As a result, the proportion of young adults with a favourable histology has increased. These changes may partly explain the increased patient survival observed both in the national and the hospital population. The hospital population comprised 92% of patients aged 15–39 years, 80% of patients aged 40–59 years and 53% of patients aged > 60 years in the national population. The selection of younger patients in the hospital material may explain a higher survival rate as compared with the national population. © **1997 Elsevier Science Ltd.**

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INTRODUCTION

IN CONTRAST to a steady increase in the reported incidence of non-Hodgkin's lymphoma (NHL), the incidence of Hodgkin's disease (HD) is stable or decreasing [1–4]. This may reflect a true decrease in incidence or due to changes in diagnostic accuracy. Epidemiological studies from all Scandinavian countries have reported a decreasing incidence of HD [1–3]. In the United States, the National Cancer Institute incidence data for 1969–1980 showed substantial declines in the HD incidence rates for persons older than 40 years and increasing incidence among young adults [5]. These results were confirmed by a later update in 1984 after correcting for age, sex and histological subtypes [6]. The incidence in older patients declined, whilst the incidence in younger adults with nodular sclerosis increased. After re-examination of histological diagnoses by an expert panel, the incidence in older adults was lower, but in young adults with nodular sclerosis, the incidence rate was slightly higher as compared with uncorrected data.

This study of a population-based registry was initiated to examine reasons for the declining incidence of HD observed in Norway since 1980.

PATIENTS AND METHODS

All patients with cancer in Norway including those with HD are registered in the Cancer Registry of Norway. This registry gives information on histological subtype according to the Rye nomenclature, sex and age at diagnosis. To obtain information on trends in this national material, 5 year periods were selected from 1971 to 1993. The hospital material included all patients admitted to the Norwegian radium hospital (NRH) Norway, over the same period as in the population-based material. In 1971–1980, the treatment of HD was centralised to the NRH as the only department for medical oncology and radiotherapy in Norway. Since 1981, four

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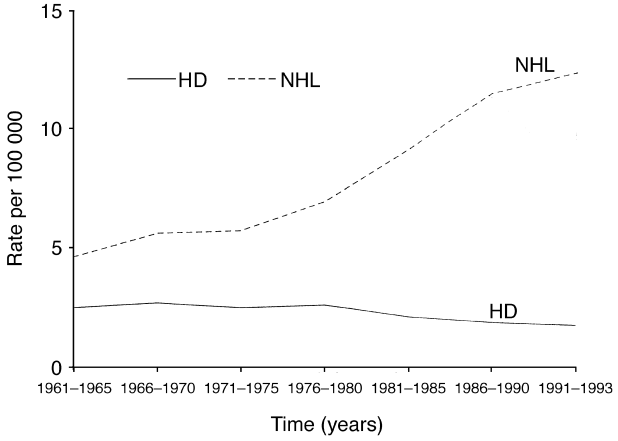

Figure 1. Average annual age-specific incidence rates of HD and NHL in Norway between 1961 and 1993.

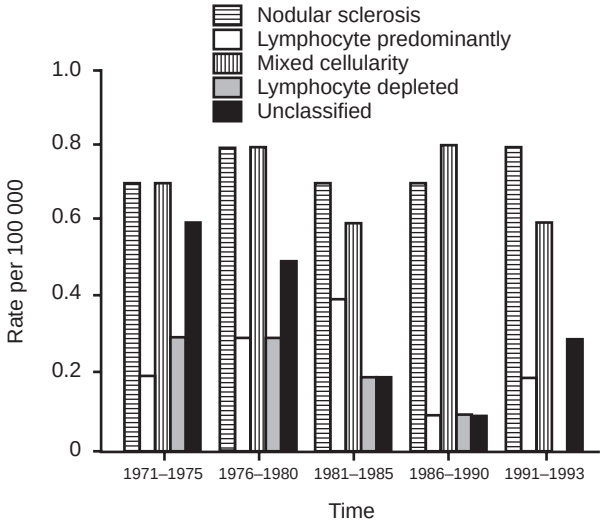

Figure 2. Average annual age-specific incidence rates of histological subgroups of HD and time period in the national material.

additional regional oncological centres gradually began to treat HD following the same protocols for staging and treatment as used at NRH. All cases admitted to NRH had biopsies re-examined by an experienced pathologist at our hospital and classified according to the Rye nomenclature. If necessary, a second biopsy was taken for further pathological and immunological examination.

Statistics

In addition to simple summary measures such as incidence rates, we estimated Kaplan–Meier survival curves using SPPS for Windows with default options [7]. Five-year survival rates are based on such curves.

RESULTS

The national material

The incidence of NHL and HD in Norway since 1961 is shown in Figure 1. The incidence of NHL has increased steadily. In contrast, the incidence of HD was stable until it decreased slightly after 1980. The clinical characteristics of all the cases of HD registered in Norway in five periods from 1971 to 1993 are shown in Table 1. The mean annual number decreased from 109 cases in 1976–1980 to 84 cases in 1986–1990 and 79 cases in 1991–1995. There was a parallel reduction in the number of men and women with HD.

Histology. The incidence rates of nodular sclerosis and mixed cellularity were relatively stable in the period studied (Figure 2). We have no explanation of the low percentage of nodular sclerosis in Norway compared with BNLI and EORTC data. In contrast, the average annual age-specific incidence of lymphocyte-depleted HD and unclassified HD decreased from 0.3 to 0 and from 0.6 to 0.3, respectively. Due to these changes in histology, the percentage of nodular sclerosis and mixed cellularity increased from 27 to 38% and from 29 to 43%, respectively. In contrast, lymphocyte-depleted HD and unclassified HD decreased from 12 to 4% and from 24 to 8%, respectively. Lymphocyte-depleted and unclassified HD were dominant in older patients. In the period studied, 82% of lymphocyte-depleted HD and 78% of unclassified HD were seen among patients > 40 years of age.

Age. The changes in age distribution at different time periods are shown in Figure 3. The average annual rates per

Table 1. *Characteristics of the registry material of HD in Norway for five-year periods between* 1971 *and* 1995

Periods	1971–1975 No. (%)	1976–1980 No. (%)	1981–1985 No. (%)	1986–1990 No. (%)	1991–1995* No. (%)
Total	511	547	459	421	397
No./year	102	109	92	84	79
Male	310 (61)	326 (60)	278 (61)	246 (58)	250 (63)
Age					
< 15 years	11 (2)	19 (4)	23 (5)	11 (3)	15 (4)
15–39 years	158 (31)	203 (37)	195 (42)	204 (49)	217 (55)
40–59 years	137 (27)	110 (20)	84 (18)	79 (19)	75 (19)
> 60 years	205 (40)	215 (39)	157 (34)	127 (30)	90 (23)
Histology					
Nodular sclerosis	138 (27)	156 (29)	156 (34)	161 (38)	160 (40)
Lymphocyte predominance	44 (9)	57 (10)	78 (17)	35 (8)	38 (10)
Mixed cellularity	147 (29)	159 (29)	140 (31)	177 (42)	128 (32)
Lymphocyte depleted	59 (12)	69 (13)	39 (8)	15 (4)	9 (2)
Unclassified	123 (24)	106 (19)	46 (10)	33 (8)	62 (16)

*Calculated from observations in 1991, 1992 and 1993.

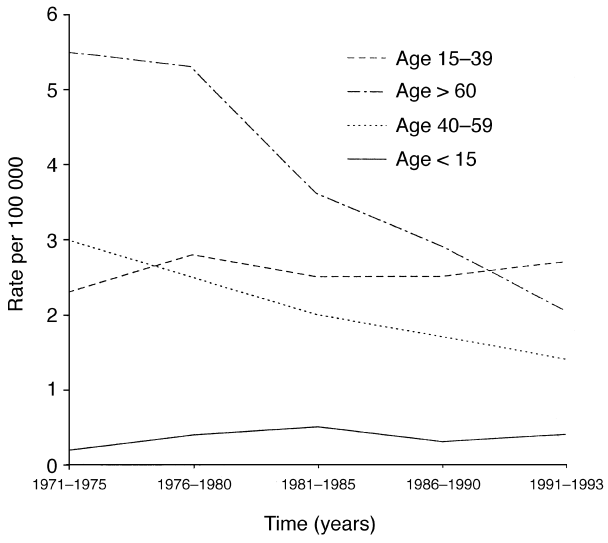

Figure 3. Average annual incidence rates of HD by age and time period in Norway.

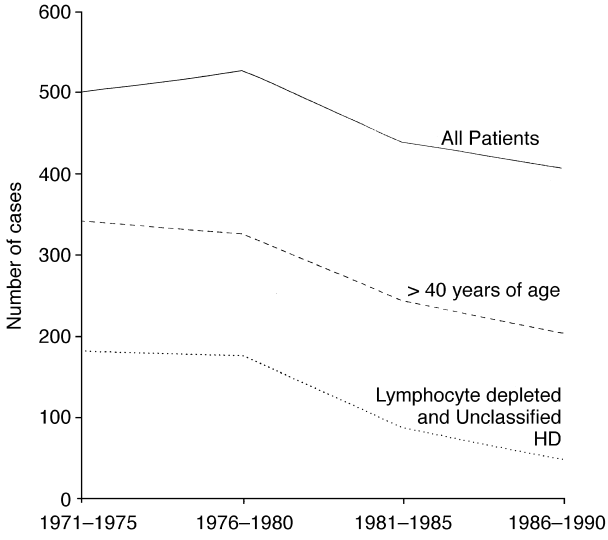

Figure 4. The number of registered cases of HD in Norway in 1971–1990.

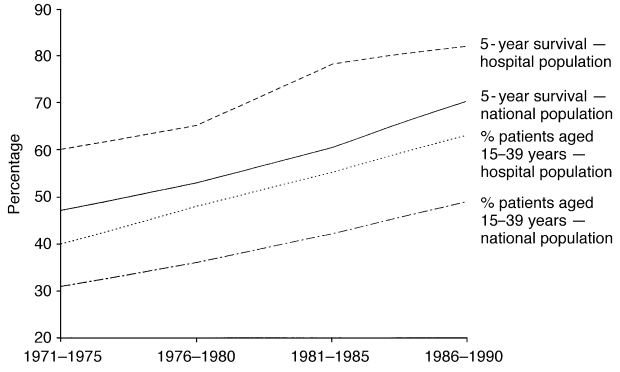

Figure 5. Survival data and age of HD patients, 1971–1990.

100 000 of patients aged < 15 years were stable and for patients 15–39 years old the rates increased from 2.3 in 1971–1975 to 2.7 in 1991–1993. For patients aged 40–49 years, 50–59 years and > 60 years the rates decreased from 2.9 to 1.7, from 3.1 to 1.2 and from 5.5 to 2.0, respectively, during the same time period. As a result, the proportion of patients aged 15–39 years increased from 31 to 49%, the proportion of patients aged 40–59 years decreased from 27 to 19%, and the proportion of patients aged > 60 years decreased from 40 to 30% of the total population during the same period.

The most interesting changes in HD population observed after 1980 were a decrease in number of diagnosed cases of HD and changes in distribution of histological subgroups and age. As seen in Figure 4, the reduced incidence of HD corresponded to the decreased incidence of patients aged > 40 years and the decreased incidence of unclassified and lymphocyte-depleted HD.

Survival. The observed 5-year survival rate increased in the observation period from 47.2 to 70.3% in all patients, from 81.2 to 89.5% in those aged 15–39 years, from 45.9 to 78.2% in those aged 40–59 years and from 21.1 to 32.8% in those aged > 60 years. Patients with lymphocyte-depleted HD and unclassified HD had an observed 5-year survival of 27.6 versus 79.1% in nodular sclerosis. As seen in Figure 5, the increase of observed survival corresponded to the increase in percentage of patients aged 15–39 years.

The hospital material

In the 1970s, the treatment of HD in Norway was centralised to the NRH. In this period, 75% of all cases diagnosed in Norway were admitted to this hospital, 92% of patients aged 15–39 years, 80% of patients aged 40–59 years and 53% of patients aged > 60 years. After 1980, an increasing number of HD patients were treated at the other university hospitals, and the annual number treated at the NRH decreased from 75% of cases registered in Norway in 1971–1980 to 40% in 1991–1993. The changes in histological subgroups of the hospital population were to some extent parallel to the changes of the national population (Figure 5). The proportion of patients aged 15–39 years increased from 38 to 70% of the hospital patients in the period studied, parallel to the relative increase of the same age population in the national population. A corresponding improvement was also observed with regard to survival (Figure 5). The changes in histological subgroups as described in the national population and the selection of younger patients to the hospital population may explain the high percentage of young adult patients with a good prognosis in the hospital population. The 5-year observed survival rate in the hospital population increased in the period observed from 60 to 82%.

DISCUSSION

We have shown that the incidence of NHL has increased steadily during the last 30 years. In contrast, the incidence of HD was almost unchanged in the 1960s and 1970s. A decreased incidence of HD after 1980 corresponded to a reduction in lymphocyte-depleted and unclassified HD. As these histologies are predominantly seen in patients > 40 years, the incidence in middle aged and older patients decreased. In spite of the decreased incidence of HD in the 1980s, the incidence in young adults has increased. The incidence of nodular sclerosis, lymphocyte predominance and mixed cellularity has been almost unchanged, but due to the

reduced incidence of lymphocyte-depleted and unclassified HD, the proportions of these histologies increased.

The main reason for the decreased incidence of HD since 1980 is most likely better diagnostic tools due to progress in immuno-histochemistry for diagnosis of borderline cases between HD and NHL [8–10] and not due to true changes in incidence. Cases previously diagnosed as lymphocyte-depleted and unclassified HD have, since 1980, been classified as NHL. As a consequence, the incidence of these histologies has decreased. The improved prognosis of HD observed during the same period is not only a result of improved treatment, but also due to an altered distribution of histopathological subgroups. The concurrent presence of older age and poor risk histology, such as lymphocyte-depleted and unclassified HD, contributed considerably to the worse prognosis in older patients. Since the percentage of younger patients with favourable histological subtypes has increased since 1980, we have also observed an improved survival rate. Thus, the nearly total elimination of the lymphocyte-depleted and unclassified subtypes may, to a considerable extent, explain the decreasing number of cases of HD since 1980, the decreasing number of older and middle aged patients, a higher percentage of younger patients and an improved survival rate.

Since 1980 these results have been obtained on routine histological diagnosis, in contrast to other studies reporting the same changes after a second classification by an expert panel [5, 6, 11–20].

Glaser and Swartz [6] demonstrated, in a study of the National Cancer Institute incidence data of HD during 1969–1984, a declining incidence of HD in older adults and an increased incidence of young adults with nodular sclerosis subtype. By using corrected histological diagnoses from the Repository Center for Lymphoma Clinical Studies, they recalculated HD incidence data. The percentage of original HD diagnoses confirmed on review of histology decreased with age and increased over time. The potential role of accurate diagnosis and classification in HD incidence is suggested by other investigators. Investigations of diagnostic accuracy have revealed overidentification of HD ranging from 6 to 47% of cases [11–20]. Three population-based studies detected the greatest diagnostic error in older persons [12, 13, 15]. Thus, HD seems to be overdiagnosed, particularly in the older age groups in which NHL is most frequent.

We have, in this study, shown the hospital population to be selected as compared with the national registry population, with a higher proportion of young patients with favourable histology. As a result, the survival rate in the hospital population was higher as compared with the national population. Ninety per cent of the young adults in the registry material were included in the hospital material as opposed to only 50% of older adults. This selection of younger patients may be explained by the fact that many older patients had widespread disease and a poor performance status and were therefore not selected for treatment with radiation or combination chemotherapy. Most clinical studies of HD are based upon more or less selected hospital populations including an increased number of young patients with a favourable stage and histology. Therefore, they do not give a correct estimate of survival in HD in an unselected population.

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