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INCREASED MORTALITY IN DUPUYTREN'S DISEASE

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A previous study showed a dip in the prevalence curve of Dupuytren's disease in men over 79 years of age. This may indicate increased mortality. The aim of the present investigation was to study this hypothesis. Four hundred and twenty-six men with Dupuytren's disease, born between 1900 and 1924 were followed for 26 years (1969–1996). Their mortality was compared with that of an age-matched control group of 426 men. In 1996, 361 with Dupuytren's disease and 336 in the control group had died. Overall, patients with Dupuytren's disease had a significantly increased mortality of 22%. The mortality was highest among those with onset of disease before the age of 60. In this age group men with Dupuytren's disease had 70% higher mortality than that of the control group. Disease duration did not seem to influence the mortality.

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When screening 15 950 persons aged 16 or older in 1969 at Haugesund, Norway, Mikkelsen (1972) found Dupuytren's disease, of some degree, in 254 women and 647 men. The diagnosis was made using conventional diagnostic criteria of typical subcutaneous nodules and bands with or without contractures of fingers. A dip was found in the prevalence curve in men over 79 years of age and women over 85 years of age (Fig 1). If this dip really reflects the epidemiological pattern of the disease in the total population, it could be caused by one of two reasons (or both): increased mortality in elderly individuals having Dupuytren's disease, and/or complete regression of the disease in a substantial number of the elderly. Schneider (1964) found spontaneous regression in some diabetic persons with Dupuytren's disease. Mikkelsen (1972) reported that a small number of persons with Dupuytren's disease stated that the finger contracture had decreased appreciably after retirement from work. Furthermore, Mikkelsen (1977b) reported that in men, the finger contracture generally increased during the first 20 years of the disease, followed by a stationary phase of about 15 years, and then tended to decrease. If a regression of the disease caused the dip in the prevalence curve, the requirement must be a total regression leaving no trace. We have not found reports of a regression of this kind, or any report about mortality in Dupuytren's disease. The present study was designed to assess whether men with Dupuytren's disease have an increased mortality rate.

METHODS

Some disease variables differ significantly between men and women with Dupuytren's disease. These include age at onset (Mikkelsen, 1977a), mean stage of finger contracture (Mikkelsen, 1976), occurrence of knuckle pads (Mikkelsen, 1977b) and age for the dip in the prevalence curve (Mikkelsen, 1972). Hence a pooling of men and women into one group was not justifiable. Only the male patient group was large enough for the present analysis, and hence this group was chosen.

For the study to have a 90% power of detecting a true relative mortality of 1.3 between men with and without Dupuytren's disease as statistically significant ($P < 0.05$), it was calculated that at least 786 men must be included (Parmar and Machin, 1995). By selecting men with Dupuytren's disease born between 1900 and 1924 from the original 1969 study of 15 950 persons, a group of 426 men aged between 45 and 69 years was available (Table 1). A match for each of the 426 was drawn at random from the 1969 material without Dupuytren's disease. Thus, every man with Dupuytren's disease was matched with a control individual without the disease born in the same year, giving a total of 852 men, which was above the required minimum.

The incidence of Dupuytren's disease within the age limits of the present sample was very high (Mikkelsen, 1972; 1977a). On a rough calculation, about 25% of the control group could develop Dupuytren's disease within the first 15 years of observation. Accordingly, an observation period of 15 years was found more appropriate for comparison than 26 years.

Permission to collect mortality data from official registers was obtained from the Norwegian Bureau of

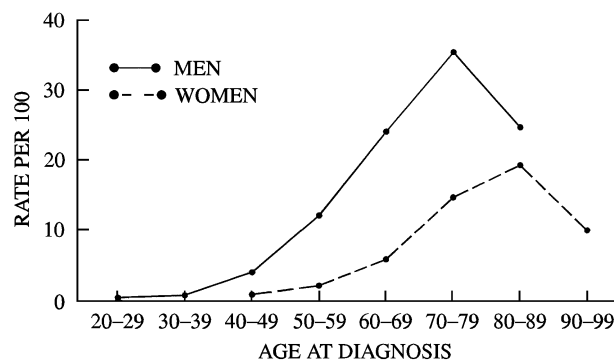


Fig 1 The prevalence of Dupuytren's disease in Norway, from a screening of 15 950 persons over 16 years of age. Reproduced by the kind permission of Acta Chirurgica Scandinavica, from Mikkelsen (1972).

Data Supervision, and these data were collected until the end of 1996.

Statistical analysis

To compare mortality in men with and without Dupuytren’s disease after adjusting for age, the Cox regression analysis was applied, with time until death as a dependent variable (Parmar and Machin, 1995). This method was also applied when comparing men with short and long duration of Dupuytren’s disease. The results obtained with this model are presented as relative risks (RR). The Kaplan-Meier method was used to estimate the survival curves in men with or without Dupuytren’s disease at screening.

RESULTS

At the end of 1996, 361 in the Dupuytren’s disease group and 336 in the control group had died. According to the Cox regression analysis, the mortality was 22% higher in the patient group than in the control group (RR = 1.22; *P* = 0.007) (Fig 2).

Table 1—Number of men with Dupuytren’s disease by age and disease duration at screening in 1969. There was an equal number of controls in each age group

Age (years)	Patients (n)	Median duration (years)
45–50	49	
51–55	82	6
56–60	95	
61–65	104	8
66–69	96	
Total	426	

The following results are based upon an observation period of 15 years after 1969. To see if the age of onset had any impact upon the mortality, the material was divided in two groups; those over 60 years and those aged 60 or less at screening. There were 200 and 226 patients and controls in each group, respectively. The mortality difference between the groups was highest among men who developed the disease before 60 years of age, and it remained high during the first 15 years of observation (RR = 1.7; *P* = 0.008) (Fig 3). Men who developed the disease after 60 had only a slightly increased mortality (RR = 1.1; *P* = NS) (Fig 4).

The impact of duration of disease on mortality was also studied. In the groups aged 45–60 (*n* = 226) years at screening, the median disease duration was 6 years (Table 1). There was no significant mortality difference

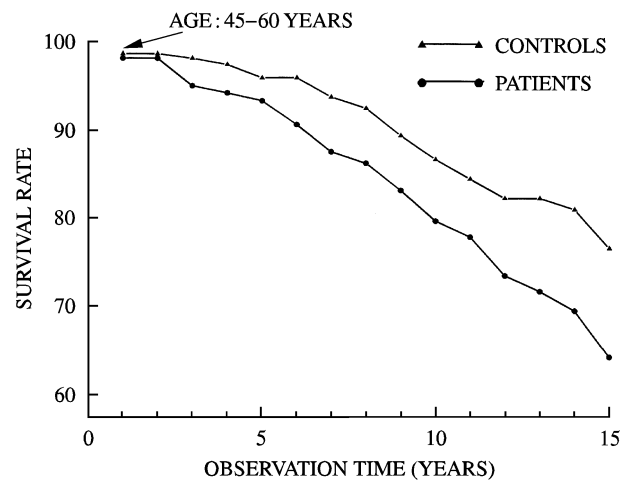


Fig 3 Survival rates of 226 patients with Dupuytren’s disease and 226 controls aged 60 or under, 1969–1984.

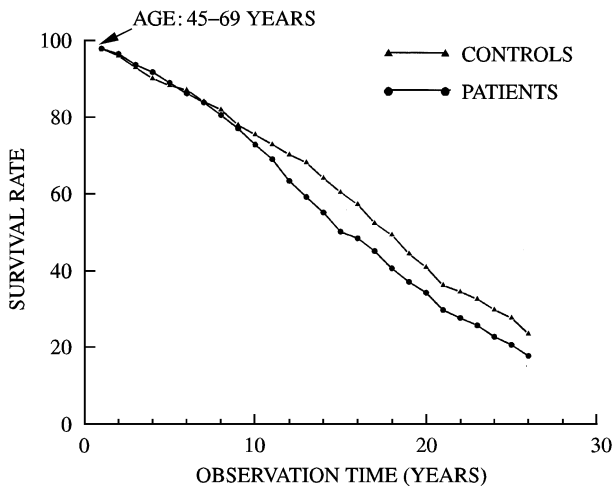


Fig 2 Survival rates of 426 patients with Dupuytren’s disease and 426 controls for the years 1969–1996.

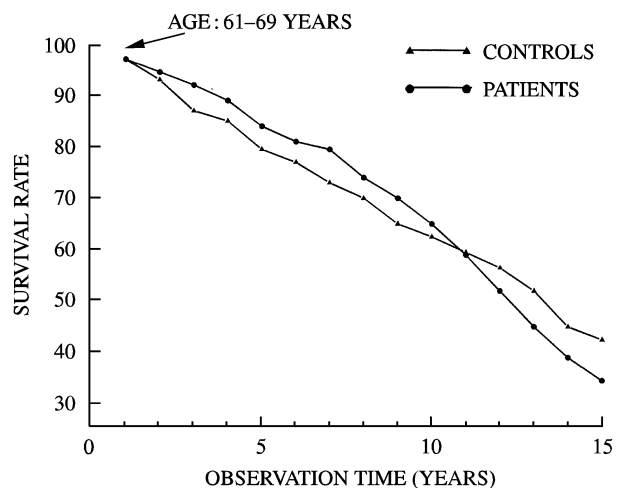


Fig 4 Survival rates of 200 patients with Dupuytren’s disease and 200 controls aged over 60, 1969–1984.

when the group with a duration of disease of 6 years or less was compared with the group with disease for more than 6 years (RR = 1.04, $P = \text{NS}$). In the group aged 61–69 ($n = 200$) years at screening, the median disease duration was 8 years. A comparison of the mortality of those with duration of disease of 8 years or less with those who had the disease for more than 8 years revealed no significant difference (RR = 1.22, $P = \text{NS}$).

DISCUSSION

This study was confined to men with Dupuytren's disease. The same dip in the prevalence curve which initiated the study was, however, also present in women, only occurring 5 to 10 years later in life than for the men (Fig 1). Therefore, the increased mortality demonstrated in men with Dupuytren's disease in the present study, is probably also valid for women.

In the analysis of the representativity and non-response in his epidemiologic survey, Mikkelsen (1972) could not find any factors causing obvious biases. He called attention to three circumstances that in theory might have caused the observed prevalence of Dupuytren's disease to be somewhat too low, but any shift would be small. The attendance rate was at least 75% for men 35 to 84 years of age. The present sample is within this age range. The present investigation is a prospective study of an unbiased sample from this material.

The possibility of a considerable number in the control group developing Dupuytren's disease during the observation period might increase the mortality rate in this group. The factor was considered to be negligible during the first part of the observation period, but would increase substantially with time. Hence, it was thought that an analysis of the mortality pattern during the first 15 years would give a more correct figure of mortality differences than if the results were based upon the longest available observation period of 26 years.

The difference in mortality in men who developed Dupuytren's disease before the age of 60 at screening, compared with men who were older, seems to support the theory that there are two types of Dupuytren's disease: one affecting younger people, showing a strong hereditary tendency; and one with no or less hereditary influence, usually starting later in life (Mikkelsen, 1990). The increased mortality seems confined to patients with the hereditary type of Dupuytren's disease.

The dip in the prevalence curve in men older than 79 years which initiated the present study, was puzzling. The prevalence curve is modified by the incidence of the disease and the variance of mortality in the patient group. A high incidence increases the prevalence. Nil incidence tends to stabilize the prevalence, whereas increased mortality tends to reduce it. The increased mortality in those under 79 years of age was probably concealed in the prevalence curve, because of the high

incidence of the disease (Mikkelsen, 1972; 1977a). The incidence in those over 79 years of age was negligible. Even a small increase in the mortality could produce the dip in the prevalence curve in this age group.

The increased mortality did not seem to be influenced by the duration of the disease. This observation reduces the possibility that some characteristic of Dupuytren's disease itself may be the cause. This would be very difficult to support by our present understanding of the pathology of this disease as a localized affection of connective tissue. The causes must probably be sought elsewhere.

Sanderson et al. (1992) found increased levels of blood lipids in patients with Dupuytren's disease. This observation is, so far, unconfirmed. If true, it might account for the increased mortality, at least to some extent.

Many authors in their search of aetiological or triggering factors, have tried to find associations between Dupuytren's disease and other diseases, such as diabetes mellitus, epilepsy and alcoholism (Hurst and Badalamente, 1990). Lately, even tobacco smoking has been found to be associated with the risk of developing Dupuytren's disease (Burge et al., 1997). All of these conditions are associated with reduced life expectancy, and a coupling to any, or perhaps all, of them might perhaps explain the increased mortality. There is, however, still some scepticism whether these associations really exist or not, except the association with epilepsy, which was well documented by Lund (1941).

The causes of death were not included in this investigation. Such information is therefore not available. This topic calls for further investigations.

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