

Epidemiology of Dupuytren's disease Clinical, serological, and social assessment. The Reykjavik Study

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Abstract

Dupuytren's disease or palmar fibromatosis is a common disabling hand disorder, mainly confined to Caucasians of northwestern European origin. The prevalence of Dupuytren's disease and possible risk factors related to the disease were evaluated in a random sample of 1297 males and 868 females, aged 46 to 74 years. Blood samples were collected and biochemical parameters were evaluated. The possible relation between the disease and clinical, social, and biochemical parameters were estimated with age-adjusted univariate logistic regression analysis. Altogether 19.2% of the males and 4.4% of the female participants had clinical signs of Dupuytren's disease. The prevalence increased with age, from 7.2% among males in the age group 45–49 years up to 39.5% in those 70–74 years old. The more severe form of the disease, finger contractures, was found in 5.0% of the men and 1.4% had required operation, while this was rarely seen among women. In men elevated fasting blood glucose ($P < 0.04$), low body weight, and body mass index were significantly correlated with the presence of the disease ($P < 0.001$). Dupuytren's disease was common among heavy smokers ($P = 0.02$) and those having manual labor as occupation ($P = 0.018$). These results show that Dupuytren's disease is common in the Icelandic population and occupation and lifestyle seem to be related to the disease. © 2000 Elsevier Science Inc. All rights reserved.

Keywords: Dupuytren's disease; Prevalence; Biochemistry; Smoking; Weight; Occupation

1. Introduction

Dupuytren's disease bears the name of the French surgeon Guillaume Dupuytren, who described it in a now famous article in *Lancet* in 1834 [1]. The disease is characterized by fibromatous nodule formations in the palmar fascia leading to finger contractures, leaving the hand with deformity and diminished function. Knuckle pads, fibrous formation in the plantar fascia (Mb. Ledderhose), and fibrous changes in the penis (Mb. Peyronie's) are believed to be related conditions [2]. Conventional treatment of Dupuytren's disease is surgical correction, but recurrence rate is high and finger amputation may be rarely be required [3]. Dupuytren's disease has a strong family tendency, and an autosomal dominant mode of inheritance has been suggested [4]. The disease is particularly common in northwestern Europe [5–9]. It has been postulated that it may initially have

spread over the northern parts of Europe during the Viking period [10]. The disease is common among offspring of immigrants from Northern Europe living in other continents [11–13]. In contrast, Dupuytren's disease is unusual in other ethnic groups such as Chinese and Africans, where it is described as sporadic finding [14,15]. The disease affects mainly men and is, in general, believed to be uncommon among young women [8,13]. Several reports have suggested association between Dupuytren's disease and other diseases and various risk factors. A positive association with non-insulin-dependent diabetes mellitus [16,17] and epilepsy [18,19] has been reported, while Dupuytren's disease is uncommon among rheumatoid arthritis patients [20]. Smoking [21,22], high levels of cholesterol and triglycerides [23], and arcus senilis [24] have also been associated with Dupuytren's disease in some studies. Other studies have indicated that manual work, especially with vibrating instruments, may predispose to the disease [25,26], but the current opinion does not support the association between manual labor and Dupuytren's disease [27,28]. The aim of

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this study was to estimate the prevalence of Dupuytren's disease in the Icelandic population and to evaluate the relation between the disease and factors supposed to predispose to the disease.

2. Patients and methods

2.1. Geology and population

Iceland is an island in the North Atlantic Ocean with a population of approximately 270,000 inhabitants. The country was settled during the Viking period (874–930), mostly from the west coast of Norway and Ireland. The population remained isolated during the Middle Ages with almost no additional immigration. Today approximately half of the population lives in the capital, Reykjavik, and surrounding area.

2.2. Design of The Reykjavik Study

The present study is a part of The Reykjavik Study [29], which is a population-based prospective cohort study of randomly selected individuals born between 1907 and 1934 living in the Reykjavik and adjacent communes. The randomized selection procedure used was based on year and day of birth. The study period extended from 1967 to 1991 and included 9128 males and 9759 females aged 34–79 years. The cohort was divided into six groups, which were invited for examination one to five times; this amounted to 32% of this birth cohort in Iceland and 45% of those living in the Reykjavik area. All participants received a letter of invitation and a questionnaire about their past and present health and social situation. A specially trained secretary checked the questionnaire with the participants. The study took place at the Heart Preventive Clinic in Reykjavik. During the visit the subjects had a clinical examination and blood samples were collected for measurement of several biochemical markers.

2.3. Study of Dupuytren's disease

During a 2-year period a total of 1297 men and 868 women were examined for signs of Dupuytren's disease. The hands of all participants were clinically examined for signs of the disease and graded into two stages. Patients with stage 1 had palpable nodule(s) in the palms, while patients with stage 2 had contracture of the fingers or had been operated on for contracture. All 2165 participants were examined by the same physician (N.S.). Height and weight were measured at arrival. Blood pressure was measured first by a nurse and about 10 days later by the physician and the average of the two measurements recorded. Participants were classified for 100 different occupations. In the study on Dupuytren's disease, we focused on manual workers (seamen, farmers, and laborer) and tradesmen (carpenters, blacksmiths, masons) and men in professions demanding higher education. In the statistical evaluation we compared each group with all other men in the cohort and adjusted for

age. Then we analyzed the relation between signs of Dupuytren's disease and age, smoking, and different occupational groups in a multivariate regressions analysis. Participants who did not have signs of Dupuytren's disease at the clinical evaluation are referred to as the reference cohort in the text and tables.

2.4. Laboratory tests

Blood samples were collected for laboratory evaluation, including hemoglobin, erythrocyte sedimentation rate (ESR), blood glucose (fasting and 90-min tolerance test), triglycerides, and total cholesterol. External and internal laboratory quality controls were used, including duplicated assays and pooled serum for interassay variation as well as control serums. The same method and instruments were used in all stages of the health survey [30].

2.5. Statistics

Univariate logistic regression analysis with age adjustment was used to evaluate statistical significance. Multivariate logistic regression was used in the analysis of social factors. The level of significance was set at $P < 0.05$.

65/249 (26%) had contractures
18/249 (7%) had prior surgery
184/249 (74%) nodules only

3. Results

3.1. Prevalence of Dupuytren's disease

Among the 1297 men examined, 249 (19.2%) had definite signs of Dupuytren's disease (Table 1). Of these 65 (5%) had stage 2 of the disease: 47 had contracture of finger(s) and 18 had been operated on for Dupuytren's disease. In 184 cases only palmar nodules could be found on palpation (stage 1). The prevalence of the disease increased significantly with age from 7.2% in men aged 45–49 years to 39.5% among those 70–74 years old. The disease was much more rare among the 868 women. Only 38 (4.4%) had any signs of the disease of which most ($n = 31$) were 60 years or older (Table 1). The left and right hands were equally often affected in both sexes.

Table 1
Age stratification of Dupuytren's disease in the study cohort

Age	Men			Women		
	Total examined	With stage 1	With stage 2	Total examined	With stage 1	With stage 2
45–49	249	13 (5.2)	5 (2.0)	131	–	–
50–54	368	46 (12.5)	9 (2.4)	188	2 (1.1)	–
55–59	259	33 (12.7)	11 (4.3)	202	5 (2.5)	–
60–64	109	19 (17.4)	9 (8.3)	117	7 (6.0)	–
65–69	193	38 (19.7)	19 (9.8)	135	13 (9.6)	3 (2.2)
70–74	119	35 (29.4)	12 (10.0)	95	7 (7.4)	1 (1.0)
All ages	1297	184 (14.2)	65 (5.0)	868	34 (3.9)	4 (0.5)

Number and percentages (in parentheses) of men and women with palmar nodules (stage 1) and contracture (stage 2) in each age group.

Table 2
Clinical status among men with Dupuytren's disease and the reference cohort

Clinical findings	Dupuytren's disease (n = 249)	Reference cohort (n = 1048)	Odds ratio (95% CI)	P value
Mean age (years)	60.8 (8.3)	56.0 (7.6)	1.07 (1.05–1.09)	<0.001
Systolic blood pressure (mmHg)	141.2 (23.0)	138.6 (20.1)	0.99 (0.98–1.00)	0.12
Diastolic blood pressure (mmHg)	87.9 (10.2)	88.5 (10.5)	0.99 (0.97–1.00)	0.07
Arcus senilis	0.42 (0.49)	0.28 (0.45)	1.15 (0.83–1.58)	0.40
Weight (kg)	76.5 (10.8)	81.9 (12.8)	0.97 (0.96–0.98)	<0.001
Height (cm)	175.6 (6.1)	177.0 (6.2)	0.98 (0.96–1.01)	0.16
Body mass index	25.0 (3.3)	26.1 (3.7)	0.91 (0.88–0.96)	<0.001

Mean values with standard deviations in parentheses are shown. Odds ratio calculated with logistic regression analysis, adjusted for age.

3.2. Clinical findings in men with Dupuytren's disease

Men with Dupuytren's disease had a mean weight of 76.5 kg, compared to 81.9 kg for those without any signs of the disease (OR = 0.97; $P < 0.001$). Men with the disease had a mean body mass index of 25.0 compared to 26.1 for those without the disease (OR = 0.91; $P < 0.001$). Height, blood pressure, or arcus senilis were not statistically associated with Dupuytren's disease (Table 2).

3.3. Biochemical markers in men with Dupuytren's disease

The mean fasting blood glucose level in men with Dupuytren's disease was 84.7 mg/dl compared to 81.1 mg/dl for the others (OR = 1.01; $P = 0.04$). However, no significant correlation was found for the glucose tolerance test after 90 min; mean value for Dupuytren's patients was 112.6 mg/dl compared to 104.1 mg/dl for the reference group (OR 1.00; $P = 0.40$). Neither diabetes mellitus nor family history of diabetes was found to be more prevalent in the Dupuytren's group (OR = 1.40; $P = 0.26$ and OR = 1.28; $P = 0.38$, respectively). None of the other measured biochemical parameters tested—total serum cholesterol, triglycerides, or ESR—was associated with the disease (Table 3).

3.4. Social factors in men with Dupuytren's disease

Table 4 shows that among the Dupuytren's patients 15.3% (38/249) were manual workers compared to 8.6%

(90/1048) of the reference cohort (OR = 1.66; $P < 0.02$). Furthermore, 14.5% (36/249) of the Dupuytren's patients were tradesmen compared to 8.6% (90/1048) of the reference group (OR = 1.83; $P < 0.01$). Only 5.6% (14/249) of the Dupuytren's patients had a university degree compared to 11.7% (123/1048) of the reference group (OR = 0.55; $P < 0.05$). Comparison of manual workers and those with occupations demanding higher education shows that Dupuytren's disease was almost three times more common among the manual workers (OR = 2.95; $P = 0.002$).

History of smoking (ever smoked) was significantly associated with the occurrence of Dupuytren's diseases (Table 5). Most of this seemed to be attributed to heavy smoking (i.e., smoking more than 25 cigarettes every day) (OR = 2.61; $P < 0.02$).

As smoking is a risk factor for Dupuytren's disease and smoking may be more prevalent in some social groups than others, we performed multivariate regressions analysis to investigate if smoking and occupation were independent risk factors of Dupuytren's disease (Table 6). After adjustment for age and occupational status, smoking was positively associated with Dupuytren's disease (OR = 1.45; $P = 0.05$). Furthermore, after adjustment for age and smoking habits manual labor and learned trade were also significantly associated with the disease (OR = 1.75; $P = 0.01$ and OR = 1.91; $P = 0.01$, respectively). Over 100 different categories were registered in this study and after drawing them into 10 different categories we calculated the associa-

Table 3
Serum biochemical markers among men with Dupuytren's disease and the reference cohort

Biochemical markers	Dupuytren's disease (n = 249)	Reference cohort (n = 1048)	Odds ratio (95% CI)	P value
Fasting glucose (mg/dl)	84.7 (26.1)	81.1 (14.3)	1.01 (1.00–1.01)	0.04
Glucose tolerance test (mg/dl) ^a	112.6 (48.9)	104.1 (36.5)	1.00 (0.99–1.00)	0.40
Cholesterol (mg/dl)	231.0 (35.2)	234.4 (36.3)	0.99 (0.99–1.00)	0.28
Triglycerides (mg/dl)	119.8 (83.9)	121.8 (73.4)	1.00 (0.99–1.00)	0.94
ESR ^b (mm/h)	5.7 (7.5)	5.5 (8.0)	0.99 (0.97–1.01)	0.35

Mean values with standard deviations in parentheses are shown. Odds ratio calculated with logistic regression analysis, adjusted for age.

^aGlucose tolerance test after 90 minutes.

^bESR = erythrocyte sedimentation rate.

Table 4
Comparison of manual workers, tradesmen, and men with occupation demanding higher education

Occupation	Dupuytren's disease (n = 249)	Reference cohort (n = 1048)	Odds ratio (95% CI)	P value
Manual labor ^a (n = 128)	38 (15.3%)	90 (8.6%)	1.66 (1.08–2.53)	<0.02
Tradesman ^b (n = 126)	36 (14.5%)	90 (8.6%)	1.83 (1.19–2.82)	<0.01
Occupation demanding higher education ^c (n = 137)	14 (5.6%)	123 (11.7%)	0.55 (0.31–0.99)	<0.05

Numbers of men in involved occupations are shown with percentages in parentheses. The association between occupational groups and Dupuytren's disease was calculated as odds ratios by comparing each group to all other men in the study using univariate logistic regression, adjusted for age.

^aManual laborers, seamen, farmers.

^bMasons, carpenters, blacksmiths.

^cWith a university degree; includes lawyers, doctors, priests, journalists, architects, engineers, musicians, dentists, scientists, judges, etc.

tions between Dupuytren's disease and occupation, with adjustment for age and smoking habits. No further significant associations were found.

3.5. Epidemiology of Dupuytren's disease in women

The clinical, social, and biochemical variables evaluated for men were also calculated for women, but none of these reached statistical significance, probably due to the low number of women with clinical signs of Dupuytren's disease.

Discussion

In this study a high prevalence of Dupuytren's disease was found in the Icelandic population. About 40% of males over the age of 70 years had palmar modules, including 10% in this age group who had contracted fingers. This high prevalence is similar to what has previously been described both in Scotland [6] and Norway [8] (Table 7). The disorder is claimed to have strong familial tendency, so this may not be surprising as Iceland was mostly settled by people from western Norway and the British Isles. In contrast to men, Dupuytren's disease, stage 2 in particular, was rarely found among the women in our study cohort. The definition for the disease used in this report is similar as previously reported in other studies [6,8,9,11,13]. Palpable nodule in the palm is a definite sign of Dupuytren's disease while finger contractures are pathognomonic for the disease. Nodules in the palm are thought to be the initial stages of the disease, which progress to finger contractures in a period of a few

years or decades. Status after trauma and stenosing tendovaginitis are the most common differential diagnosis.

There has been an ongoing debate whether this common disabling hand deformity is caused by manual work [1,25–28]. The current opinion has in general not favored the idea of a positive relation between manual work and fibromatosis of the palm. However, we found a highly significant association between manual work and Dupuytren's disease. Furthermore, we found an inverse relation between Dupuytren's disease and professions demanding higher education, an association that was statistically significant in univariate logistic analysis (Table 4) and showed a nonsignificant trend when calculated with multivariate logistic regressions analysis (Table 6). Thus, the risk of having Dupuytren's disease was almost three times higher for manual workers compared to those with higher education.

Smoking was also significantly more common among Dupuytren's patients compared to the reference cohort. Thus, our results strongly suggest that various social factors, such as occupation and lifestyle, are important for the development of this disease. We do not have data about the alcohol use of the participants in the present study, but in previous studies of randomly selected populations no association between alcohol and Dupuytren's disease has been found [5,7,32]. However, for patients in hospital settings such associations have been proposed [33,34]. Mechanical strain or minor trauma have been thought to predispose to the disease or, as Baron Dupuytren himself pointed out: "The greater number of individuals affected by this disease have been obliged to make effort with the palm of the hand

Table 5
Relation between Dupuytren's disease in men and smoking habits

Smoking history	Dupuytren's disease (n = 249)	Reference cohort (n = 1048)	Odds ratio (95% CI)	P value
Ever smoked	0.82 (0.39)	0.77 (0.42)	1.49 (1.04–2.16)	0.03
Former smoker	0.37 (0.48)	0.33 (0.47)	1.50 (0.10–2.25)	0.05
Smoking pipe/cigars	0.19 (0.39)	0.20 (0.40)	1.30 (0.80–2.10)	0.34
Smoking 1–14 cig./day	0.08 (0.28)	0.07 (0.26)	0.80 (0.77–2.59)	0.26
Smoking 15–25 cig./day	0.11 (0.31)	0.11 (0.32)	1.36 (0.80–2.36)	0.27
Smoking >25 cig./day	0.07 (0.26)	0.06 (0.23)	2.61 (1.25–4.64)	0.02

Mean values with standard deviations in parentheses are shown. The associations between smoking and Dupuytren's disease calculated with a univariate logistic regression analysis, adjusted for age.

Table 6
Dupuytren's disease, social status, and smoking among men in the study cohort

	Odds ratio	95% CI	P value
Age	1.08	1.06–1.09	<0.01
Ever smoked ^a	1.45	1.00–2.10	0.05
Manual labour ^b	1.75	1.14–2.70	0.01
Learned trade ^c	1.91	1.24–2.96	0.01
Occupation demanding higher education ^d	0.67	0.37–1.20	0.18

Comparison of manual workers, tradesman, and men in companions demanding higher education using multivariate logistic regression analysis, adjusted for age and smoking.

^aHaving ever smoked, former and present smokers. Odds ratio adjusted for age and occupational status.

^bManual labors, seamen, farmers. Odds ratio adjusted for age and smoking habits.

^cMasons, carpenters, blacksmiths. Odds ratio adjusted for age and smoking habits.

^dMen with a university degree and working as such; includes lawyers, doctors, priests, teachers, journalists, architects, engineers, musicians, dentists, scientists, judges, etc. Odds ratio adjusted for age and smoking habits.

or frequently to handle hard bodies" [1]. It should, however, be noted that other external factors than mechanical strain or repetitive minor trauma could be causing the benign fibrosing tumors of the palm. Thus, the hands of manual workers are exposed to a number of chemical compounds and physical factors potentially capable of causing tissue damage.

In our study fasting blood glucose levels were significantly higher in the Dupuytren's group than in the reference cohort. The clinical relevance of this is uncertain, but perhaps it indicates that increased fasting blood glucose, even at subclinical values, may influence biochemical pathways involved in the formation of fibrosing nodules in the palmar aponeurosis. We found a highly significant inverse relation between Dupuytren's disease and body weight and body mass index. It has previously been suggested that elevated cholesterol and triglycerides correlate with the presence of Dupuytren's disease [23], but we were not able to find any such associations. Furthermore, in the present study, the Dupuytren's patients did not have higher blood pressure or increased prevalence of arcus senilis, compared to the reference cohort. Thus, there is no evidence in our data to support the suggestion, that patients with Dupuytren's disease have a cardiovascular disease risk profile, as has been suggested [23,24].

It has been proposed that microvascular changes are central in the pathogenesis of Dupuytren's disease [35,36]. Diminished blood flow with hypoxia may induce the release of several substances, including platelet derived growth factor (PDGF). PDGF might trigger endothelial proliferation with fibroblast transformation and increased collagen synthesis, resulting in formation of fibromatous nodules and finger contracture. The epidemiologic data presented in this report may support the suggestion that microvascular changes are connected to the pathogenesis of Dupuytren's disease. We observed a higher risk of the disease among

Table 7
Previous studies describing the prevalence of Dupuytren's disease

First author year [ref.]	Selected group/country	Diagnostic criteria	Number examined	Prevalence/comments
Gordon 1954 [12]	Hospital patients Canada	Not given	2705	26% of males aged 66–75 years 33% of females aged 66–75 years
Yost 1955 [11]	Hospital patients. 37% Afro-Americans. USA	Nodules in the palm, contracture of fingers.	5062	3.4% of all examined Male to female ratio 3:1 Age dependent
Hueston 1960 [13]	1. Manual workers and clerks. 2. Ill in hospital. 3. Residents in institution. Australia	Nodule of hand, in palmar facia or contracted finger	3700	23% of males older than 60 years 22% of females older than 60 years
Hueston 1962 [31]	Short term hospital patients. Australia	Flexion deformity	1226	28% of males older than 60 years 17.5% of females older than 60 years
Early 1962 [9]	1. Urban population. 2. Locomotive workers. 3. Old people's home. England	From isolated palmar nodules to the severest deformities	6979	4.2% of all males 1.4% of all females 18.1% of males older than 75 years
Mikkelsen 1969 [8]	Population sample screened for TBC, 16 years and older. Norway	Subcutaneous nodules adherent to the skin, band and contractures	16005	37% of males older than 70 years 25% of females older than 80 years
Bergenudd 1983 [7]	Population study Sweden	Physical examination with special attention to occurrence's of Dupuytren's contractures	574	10% of males aged 55 years 2% of females aged 55 years
Lennox 1993 [6]	Geriatric patients Scotland	Palmar or plantar nodules or skin tethering, contractures	200	39% of males older than 60 years 21% of females older than 60 years
Present study	Randomly selected population Iceland	Nodule in the palm or contracted finger	2165	19.2% of males aged 46–74 years 4.4% of females aged 46–74 years

smokers and men with high blood glucose levels. Both these factors are well known to affect the peripheral circulation. Dupuytren's disease was also more common among men working primarily with their hands (i.e., with occupations where instruments are used that may compress the ulnar side of the hand). The disease has a striking geographic presentation in the colder parts of northwestern Europe, so it is tempting to suggest that manual labor in cold climate may predispose to prolonged vasoconstriction in the microvasculature of the hand. The disease is more prevalent among men who are of less weight, and thus possibly less protected from the cold and harsh environment dominating in this region.

This study shows that Dupuytren's disease is common in the Icelandic population, it is highly age dependent, and associated with occupation and lifestyle. Even though Dupuytren's disease may have a familial tendency, several external factors seem to contribute significantly to the disease process and occurrence of the disease.

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