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Prevalence of joint complaints amongst individuals with Dupuytren's disease – From the Reykjavík study

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It has been reported that Dupuytren's disease is very uncommon amongst patients with rheumatoid arthritis (RA). We investigated the prevalence of different joint complaints in a cohort of 1297 males, aged 46–74 years, participating in a prospective longitudinal health survey. Joint complaints were less frequently observed in men with Dupuytren's disease than in those who did not have any signs of this disease. When adjusted for age the Dupuytren's patients had less frequently history of morning stiffness (odds ratio (OR) = 0.65; 95% confidence interval (CI) = 0.44–0.98, P = 0.04), joint swelling (OR = 0.52; 95% CI = 0.27–1.00, P = 0.05), and attendance to doctors due to rheumatic disorders (OR = 0.44; 95% CI = 0.15–0.86, P = 0.02) than those who did not have clinical signs of Dupuytren's disease. Furthermore, these associations were even stronger after adjustment for other potential confounding factors, such as smoking, lipids, diabetes, education, and occupation. The reason for a negative association between Dupuytren's disease and joint complaints is not clear but genetic and immunological factors may be important.

Key words: Dupuytren's contracture, rheumatic diseases, autoantibodies, rheumatoid factor

Dupuytren's disease is characterised by fibrosis followed by thickening and shortening of the palmar aponeurosis, eventually leading to flexion deformity of the fingers. This condition was initially described by Baron Guillaume Dupuytren in a famous article published in the Lancet in 1834 (1). The exact etiology of this condition is not known, but some risk factors have been reported, including high cholesterol and triglyceride levels, smoking, alcohol consumption, and certain types of manual labour (2–4). There are also indications that autoimmunity or dysregulation of the immune system may play a role in the pathogenesis of Dupuytren's disease. Thus, associations with certain HLA-DR subclasses have been reported, raised levels of anticollagen autoantibodies have been observed, increased T-cell infiltration, and high concentrations of IgM and IgA antibodies have been found in diseased tissues of Dupuytren's patients (5–7). Furthermore, it has been reported that local immunomodulating therapy, with steroids and interferon-γ (IFN-γ), may have a beneficial effect on Dupuytren's contracture (8–10). A positive association with certain autoimmune diseases, such as diabetes mellitus, has been reported in some studies (11, 12). In contrast, it has been found that Dupuytren's disease is very uncommon amongst rheumatoid arthritis (RA) patients (13). We evaluated the relationship between Dupuytren's disease and joint complaints in a cohort of males participating in a prospective longitudinal health survey.

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Materials and methods

Study design

The present study is part of a larger prospective health survey in Iceland focusing on cardiovascular diseases and risk factors. The study was initially started in 1967 (14). At every visit the participants answered a detailed structured health questionnaire with special emphasis on cardiovascular diseases. Included in this questionnaire were also several questions about joint complaints; joint pain and swelling, morning stiffness (>15 minutes), and attendance to medical doctors due to rheumatic disorders (15). The same physician (N.S.) evaluated all the participants for signs of cardiovascular diseases and blood samples were collected at the time of examination. In 1981, in addition to the routine processes described, a cohort comprising 1297 males representative of the population was screened for the presence of Dupuytren's disease by detailed clinical inspection and palpation of both hands. Mean age of the participants was 56.9 years (range 46 to 74 years). Before participating every subject received detailed information about the study. Furthermore, this and other parts of the study were approved by relevant authorities and ethical committees.

Rheumatoid factor testing

Blood samples from 1149 (88.6%) of the participants were tested for rheumatoid factor (RF) by the Rheumaton agglutination slide screening test (Wampole Lab, NJ, USA). Results were expressed as positive or negative. Samples positive in this screening test were tested further by the classical Waaler-Rose technique (16, 17). Seropositivity was defined as a titer $\geq$1:20.

Statistical evaluation

The Chi-square test, with Yates correction for expected frequencies less than five, was used to evaluate differences between groups. As the Dupuytren's patients were significantly older than the other participants a logistic regression analysis was performed to adjust for this age difference. The findings were also adjusted for several other possible confounding factors that previously have been associated with the prescence of Dupuytren's disease. These included smoking habits, lipid levels (cholesterol and triglycerides), diabetes, education, and occupation. The level of significance was set at $P<0.05$.

Results

Of the 1297 participants 249 (19.2%) had at the time of the clinical examination signs of Dupuytren's disease; 18 had been operated due to contractures, 47 had visible contractures of one or more fingers, and 184 palpable nodules or thickening of the palmar aponeurosis. The prevalence of Dupuytren's disease was highly age dependent (Fig. 1). Thus, the prevalence of Dupuytren's disease increased from 7.2% amongst participants <50 years of age to 39.5% amongst those who were $\geq$70 years ($P<0.0001$). Participants diagnosed with Dupuytren's disease were significantly older than the other participants; mean age 60.8 *vs.* 55.9 years.

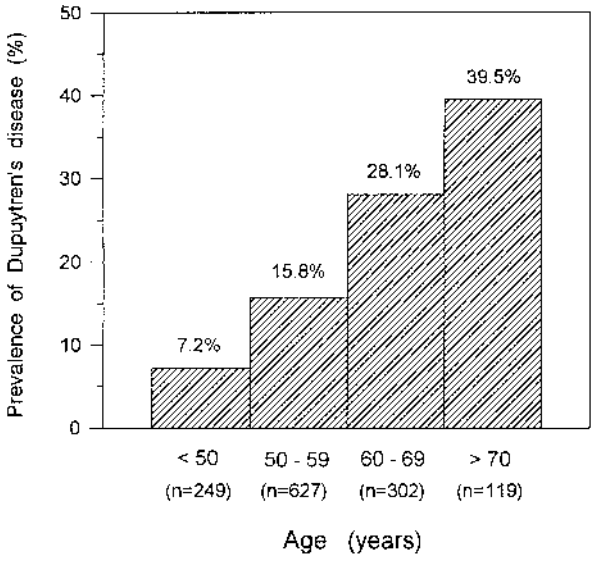

Fig. 1. Prevalence of Dupuytren's disease amongst men aged 46 to 74 years.

Table I shows the association between Dupuytren's disease and individual joint complaints. The Dupuytren's patients complained less frequently about recent joint swelling ($P=0.04$) and had also less frequently attended a medical doctor due to rheumatic disorders ($P=0.03$) than participants without Dupuytren's disease. Furthermore, morning stiffness and a positive Rheumaton test tended to be less frequent amongst the Dupuytren's patients ($P=0.06$ and $P=0.08$ respectively).

As the participants with Dupuytren's disease were significantly older than the participants without this

Table I. Prevalence of joint complaints amongst participants with and without Dupuytren's disease.

Joint complaints†	Dupuytren's disease		Significance
	No (n=1048)	Yes (n=249)	
1. Joint pain	224 (21.4%)	47 (18.9%)	P=0.38
2. Joint pains in $\geq$3 joints simultaneously	91 (8.7%)	16 (6.4%)	P=0.24
3. Joint swelling	86 (8.2%)	11 (4.4%)	P=0.04
4. Morning stiffness	196 (18.7%)	34 (13.7%)	P=0.06
5. Attended medical doctor due to rheumatic disorder	62 (5.9%)	6 (2.4%)	P=0.03
6. Positive Rheumaton test‡	132 (14.3%)	22 (9.9%)	P=0.08
7. Positive Rose-Waaler test‡	22 (2.4%)	2 (0.9%)	P=0.17

†1–5 refers to symptoms for the last 12 months before participating in the present study. Rheumatoid factor (number 6 and 7) was tested in samples collected at the time of study.
‡Rheumatoid factor was tested in 1149 (88.6%) of the participants.

Table II. Age adjusted associations between Dupuytren's disease and joint complaints.

Joint complaints†	Odds ratio‡	95% confidence interval	Significance
1. Joint pain	0.90	0.63–1.29	P=0.56
2. Joint pains in ≥3 joints simultaneously	0.71	0.40–1.24	P=0.23
3. Joint swelling	0.52	0.27–1.00	P=0.05
4. Morning stiffness	0.65	0.44–0.98	P=0.04
5. Attended medical doctor due to rheumatic disorder	0.44	0.15–0.86	P=0.02
6. Positive Rheumaton test	0.69	0.42–1.14	P=0.15
7. Positive Rose-Waaler test	0.31	0.07–1.38	P=0.12

†Questions 1–5 refer to rheumatic manifestations observed for the last 12 months before participating in the present study.
‡Logistic regression analysis, adjusted for age.

condition the age might have influenced the findings reported in Table I. Therefore, a logistic regression was performed to adjust for the age difference between the two groups (Table II). When adjusted for age the history of joint swelling (P=0.05), morning stiffness (P=0.04), and attendance to a medical doctor due to rheumatic disorders (P=0.02) were significantly less frequent amongst the participants with Dupuytren's disease than for the other participants.

Previous studies have reported a positive association between the prescence of Dupuytren's disease and factors such as smoking, cholesterol and triglyceride levels, diabetes, education, and occupation. Table III shows the associations between Dupuytren's disease and joint complaints after adjustment for these potentially confounding factors. Still, the history of recent joint swelling (P=0.04), morning stiffness (P=0.01) and attendance to a medical doctor due to rheumatic disorders (P=0.01) was significantly less frequently observed amongst the Dupuytren's patients than among the other participants. Furthermore, the Rheumaton and Rose-Waaler tests tended to be less frequently positive amongst the Dupuytren's patients (P=0.09 in both cases).

Discussion

In our study a statistically significant negative relationship was observed between Dupuytren's disease and joint complaints. Furthermore, it should also be noted that all the other joint manifestations recorded in this study were less frequently positive in the individuals with Dupuytren's disease (Table II; OR=0.31–0.90 and Table III; OR=0.28–0.82) than those without, although the differences did not reach statistical significance. Our finding is therefore in good agreement with a report by Arafa and co-workers (13) who observed low incidence of Dupuytren's disease amongst patients with RA.

Several studies have reported associations between Dupuytren's disease and certain risk factors, such as cholesterol and triglyceride levels, diabetes mellitus, smoking, and certain types of manual labour (2–4, 11, 12). All these factors might influence the associations observed between Dupuytren's disease and joint complaints. Therefore we made several adjustments to correct for these possible confounding factors (Table III). Interestingly the negative association between Dupuytren's disease and joint complaints was still statistically significant after these corrections.

Table III. Associations between Dupuytren's disease and joint complaints after adjustment for age, smoking habits, cholesterol and triglyceride levels, diabetes, education, and occupation.

Joint complaints†	Odds ratio‡	95% confidence interval	Significance
1. Joint pain	0.82	0.57–1.20	P=0.31
2. Joint pains in ≥3 joints simultaneously	0.63	0.35–1.11	P=0.11
3. Joint swelling	0.51	0.26–0.99	P=0.04
4. Morning stiffness	0.58	0.38–0.88	P=0.01
5. Attended medical doctor due to rheumatic disorder	0.30	0.12–0.77	P=0.01
6. Positive Rheumaton test	0.64	0.39–1.07	P=0.09
7. Positive Rose-Waaler test	0.28	0.06–1.23	P=0.09

†Questions 1–5 refer to rheumatic manifestations observed for the last 12 months before participating in the present study.
‡Logistic regression analysis, adjusted for age, smoking, cholesterol, triglycerides, diabetes, education and occupation.

Table IV. The prevalence of Dupuytren's disease amongst men in different studies and countries. The diagnostic criteria for Dupuytren's disease and the selection of study cohorts may differ between individual studies.

Author, year (reference)	Country	Age of study cohort (years)	Prevalence
Gordon, 1954 (22)	Canada	66–75	26%
Yost et al., 1955 (23)	USA	>30	3%
Hueston, 1960 (24)	Australia	>60	23%
Hueston, 1962 (25)	Australia	>60	28%
Early, 1962 (26)	UK	>75	18.1%
Mikkelsen, 1972 (27)	Norway	>70	37%
Thomas & Clarke, 1992 (28)	UK	50–85	10.7%
Bergenudd et al., 1993 (29)	Sweden	55	10%
Lennox et al., 1993 (30)	UK	>60	39%
Carson & Clarke, 1993 (31)	UK	65–97	13.8%
Present study	Iceland	46–74	19.2%

The reasons for a relatively low prevalence of joint complaints amongst individuals with Dupuytren's disease are not clear, but it is possible that genetics are of importance. Thus, high prevalence of HLA-DR3 has been reported in patients with Dupuytren's disease and related fibrosing disorders (5, 18). In contrast, it is well established that some rheumatic diseases such as RF positive RA are mainly associated with the HLA-DR4 antigen, but not DR3. Thus, different genetic background might possibly explain the negative association between joint complaints and Dupuytren's disease and familial aggregation of the disease has been shown (19, 20). Another explanation has also been suggested: that patients with RA do not always notice the symptoms of Dupuytren's disease (21) and this might account for the low prevalence reported in this group of patients. That report was however based on only four RA patients. Even if true it can hardly explain the differences observed in our study cohort as the differences between groups regarding clinical symptoms were also reflected by the lower percentage of Rheumaton and Waaler-Rose positivity in the Dupuytren's patients.

In our study the overall prevalence of Dupuytren's disease amongst Icelandic men aged 46 to 74 years was 19.2%. This prevalence is similar to that reported in some previous studies (Table IV). Thus, Early (26) found a prevalence of 18.1% in the United Kingdom and Carson & Clarke (31) a prevalence of 13.8%. Other studies have reported both considerably higher and lower prevalences (29, 30). Some of the differences reported might be attributed to different criteria for selection of the study cohorts (for example different age groups) and possibly also different criteria used to diagnose Dupuytren's disease. Ethnical differences might be the explanation in some cases.

Although the reason for the negative association between Dupuytren's disease and joint complaints remains to be clarified we would like to propose the following hypothesis; A distinct subset of B-lymphocytes (CD5+ cells) is important in the production of various autoantibodies, including RF production, in humans (32, 33). It is known that both CD5+ B-lymphocytes and RF are increased in RA patients and a positive correlation between CD5+ cells and elevated RF has been found in RA (34, 35). In contrast, we have previously reported that patients with Dupuytren's disease have decreased CD5+ B-lymphocytes compared to healthy controls (36). This decrease in CD5+ B-lymphocytes in patients with Dupuytren's disease is therefore in agreement with the relatively low prevalence of positive RF and joint complaints observed in the Dupuytren's patients in our study. The findings support the suggestion that immunological mechanisms may be important in the pathogenesis of Dupuytren's disease (7, 36) as well as in RA (15, 34, 35). However, different genetic background and response to triggering agents stimulates the CD5+ B-lymphocytes to be upregulated in RA while they are downregulated in Dupuytren's disease and therefore protecting against the development of RA and possibly also other rheumatic disorders.

It is concluded that the prevalence of joint complaints amongst individuals with Dupuytren's disease is low. The reasons are not clear but a combination of genetic, immunological, and environmental factors may be important.

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