



University of Groningen

Prevalence of Dupuytren Disease in The Netherlands

Lanting, Rosanne; van den Heuvel, Edwin R; Westerink, Bram; Werker, Paul M N

Published in: Plastic and Reconstructive Surgery

DOI:

10.1097/PRS.0b013e3182958a33

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version Publisher's PDF, also known as Version of record

Publication date:

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Lanting, R., van den Heuvel, E. R., Westerink, B., & Werker, P. M. N. (2013). Prevalence of Dupuytren Disease in The Netherlands. *Plastic and Reconstructive Surgery*, *132*(2), 394-403. https://doi.org/10.1097/PRS.0b013e3182958a33

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverneamendment.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 04-06-2022

HAND/PERIPHERAL NERVE

Prevalence of Dupuytren Disease in The Netherlands

Rosanne Lanting, M.D. Edwin R. van den Heuvel, Ph.D. Bram Westerink, B.Sc. Paul M. N. Werker, M.D., Ph.D.

Groningen, The Netherlands

Background: Dupuytren disease is a fibroproliferative disease of palmar fascias of the hand. The prevalence of Dupuytren disease and the association with potential risk factors have been the subject of several studies, although there is a paucity of such data from The Netherlands.

Methods: To study the prevalence of Dupuytren disease, the authors drew a random sample of 1360 individuals, stratified by age, from the northern part of The Netherlands. Of this sample, 763 individuals aged 50 to 89 years participated in this cross-sectional study. The authors examined both hands for signs of Dupuytren disease, and a questionnaire was conducted to identify potential risk factors. The effects of these risk factors were investigated using logistic regression analysis. Additional analyses were performed to develop a logistic prediction model for the prevalence of Dupuytren disease.

Results: The prevalence of Dupuytren disease was 22.1 percent. Nodules and cords were seen in 17.9 percent, and flexion contractures were present in 4.2 percent of the study population. Prevalence increased with age, from 4.9 percent in participants aged 50 to 55 years to 52.6 percent among those aged 76 to 80 years. Men were more often affected than women; 26.4 percent versus 18.6 percent, respectively (p = 0.007). Other significant risk factors were previous hand injury, excessive alcohol consumption, familial occurrence of Dupuytren disease, and presence of Ledderhose disease.

Conclusions: The results show a high prevalence of Dupuytren disease in The Netherlands, particularly the nodular form. Using the developed logistic prediction model, the prevalence of Dupuytren disease can be estimated, based on the presence of significant risk factors. (*Plast. Reconstr. Surg.* 132: 394, 2013.) **CLINICAL QUESTION/LEVEL OF EVIDENCE:** Risk, III.



upuytren disease is a benign fibroproliferative disease of some of the palmar fascias of the hand. This disease causes the formation of nodules that can eventually progress into cords, giving rise to flexion contractures of the affected fingers. Etiologic risk factors previously described include smoking, alcohol consumption, manual work, hand trauma, diabetes mellitus, and epilepsy. ¹⁻⁴ However, the role of these factors is not fully elucidated, and evidence is at times contradictory. Observations from twin studies and family studies suggest that Dupuytren disease has a strong genetic component. ⁵⁻⁷ Recently,

From the Departments of Plastic Surgery and Epidemiology, University of Groningen, University Medical Center.

Received for publication January 7, 2013; accepted February 20, 2013.

Presented in Dutch at the Biannual Meeting of the Dutch Society of Plastic Surgery, in Groningen, The Netherlands, October 5 and 6, 2012.

Copyright © 2013 by the American Society of Plastic Surgeons

DOI: 10.1097/PRS.0b013e3182958a33

in a genome-wide association study, nine genes were identified to be associated with Dupuytren disease.⁸

The disease is particularly common in northern parts of Europe^{9,10} and in countries where people of Northern European descent live. The majority of prevalence studies has been conducted in Scandinavia and in the United Kingdom. Sporadic cases have been identified in other parts of the world, such as Africa and the Far East. ^{11,12} The prevalence of Dupuytren disease has been found to vary from 0.2 to 56 percent, ¹³ indicating great heterogeneity between study populations.

Prevalence rates of Northern European countries such as The Netherlands and Germany are unknown. Because life expectancy is expected to

Disclosure: Dr. Werker is a consultant for the pharmaceutical company Pfizer. Dr. van den Heuvel is a consulantant for Merck (microbiology). The other authors have no financial interest to declare.

increase considerably in the coming decades¹⁴ and Dupuytren disease is a chronic disease of the elderly, it is becoming more important to improve our knowledge about current prevalence rates. Prevalence rates may be used to evaluate cost effectiveness of emerging treatments, such as percutaneous needle fasciotomy, collagenase injection, and radiotherapy.

The primary aim of this study was to determine the prevalence of Dupuytren disease in the general population older than 50 years in the northern part of The Netherlands. A secondary goal was to investigate the association between Dupuytren disease and potential risk factors.

PATIENTS AND METHODS

A cross-sectional study was performed using a stratified random sample by age of 1360 inhabitants older than 50 years in Groningen, The Netherlands. The ratio of the sample size and population size in each age category was the same across age categories. The sample was drawn from the municipal administration, and our results were compared with data from the central bureau of statistics, Statistics Netherlands. 15 To conduct this study, dispensation was obtained from our institutional ethics review board. If subjects were willing to participate and signed an informed consent form, we examined both hands for signs of Dupuytren disease and knuckle pads. Signs of Dupuytren disease include tethering of the skin, nodules, cords, and finger contractures in individuals with cords. If any of these features was present, the individual was labeled as having Dupuytren disease. We used the classification of Iselin to assess the severity of the disease. 16 This classification consists of four categories (Fig. 1):

- Degree I: palmar nodules and small cords without signs of contracture.
- Degree II: contracture of the metacarpophalangeal joint.
- Degree III: contracture of the metacarpophalangeal and proximal interphalangeal joint.
- Degree IV: severe contracture of the metacarpophalangeal and proximal interphalangeal joints with hyperextension of the distal interphalangeal joint, also known as a Boutonnière deformity.

In addition to examination of the hands, we inquired about smoking habits, alcohol consumption, dexterity, whether participants had performed

manual labor during a significant part of their life, and whether they had sustained hand injury in the past, including surgery. In addition, we inquired about the presence of diabetes or epilepsy; familial occurrence of Dupuytren disease, defined as a first-degree relative with Dupuytren disease; and for the presence of Ledderhose disease.

Sample Size Calculation

Sample size calculation was performed using a formula described by Daniel.¹⁷ The following unknowns were imputed into the formula: p =0.15 based on an expected prevalence of 15 percent as found in a previous pilot study (unpublished data), delta = 0.025 to define the length of the confidence interval, and a two-sided α of 0.05. Taking into account an estimated nonresponse rate of 40 percent, a sample size of 1360 individuals was calculated. Age stratification in eight categories was based on age distribution of the general population in Groningen, derived from the Statistical Yearbook 2010 of the Groningen City Council.¹⁸ Based on the calculated sample size and the age distribution, a simulation study was conducted to investigate whether the stratified sampling approach could estimate a logistic model for the prevalence of Dupuytren disease by age as precisely as would a random sample (results not provided).

Statistical Analyses

The characteristics of the collected sample were described by medians with interquartile range and by proportions with appropriate confidence intervals. The median age and proportion of men between the sample and nonresponders was tested using the Mann-Whitney U test and the Pearson chi-square test, respectively. The proportion of nonresponders across age categories was tested using the chi-square test again. The overall prevalence was calculated and categorized by disease severity. The difference in prevalence for the hands and fingers was tested with generalized estimating equations using the cumulative logit link function, an exchangeable working correlation matrix, the robust estimator, and the generalized score statistic. First, the interaction effect between hands and fingers was tested and, if not significant, the hand and finger effects were investigated separately. These effects were corrected for age categories. Odds ratios for the pairwise differences between fingers and hands were calculated if any of the three effects (fingers, hands, and interaction) would be significant at the level of $\alpha = 0.05$.

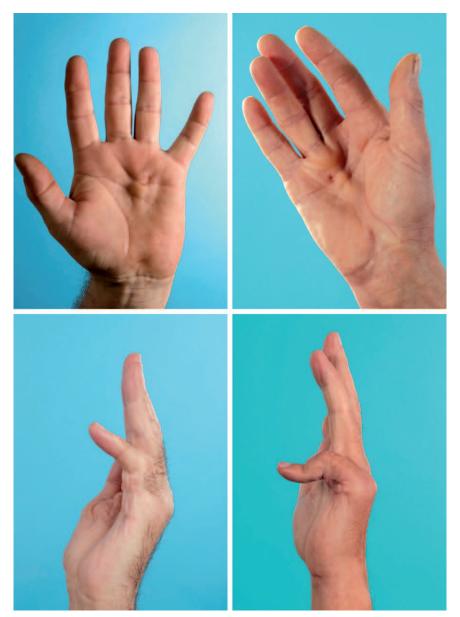


Fig. 1. Iselin classification of severity of Dupuytren disease. (*Above, left*) Degree I in ring finger; (*above, right*) degree II in ring finger; (*below, left*) degree III in little finger; and (*below, right*) degree IV in little finger.

In addition, the effects of possible risk factors on the prevalence of Dupuytren disease were investigated with logistic regression analysis. The effects of sex, diabetes, epilepsy, family history of Dupuytren disease, and presence of Ledderhose disease were corrected for age categories. The effects of manual labor, hand injury, alcohol consumption, smoking, and the presence of knuckle pads were corrected for sex and age categories in this analysis.

The final analyses were conducted to determine a logistic prediction model for the prevalence of Dupuytren disease. The risk factors with

a value of p < 0.15 from previous analysis were selected for the model, and age was taken continuous and a quadratic relation was assumed. Backward elimination using the Wald test statistic was applied at the significance level of 0.05 to develop the final model.

RESULTS

Prevalence of Dupuytren Disease

Our stratified random sample by age included 1360 individuals. In total, 763 were willing to participate: 348 men and 415 women. Population

Table 1. Population Characteristics

Participants	No. (%)	95% CI
No. of participants	763	
Women	415 (54.4)	50.9-57.9
Age, yr		
Median	62	
IQR	56-69	
Examination		
Dupuytren disease	169 (22.1)	19.2 - 25.1
Knûckle pads	116 (15.5)	12.9 - 18.1
Questionnaire		
Smoking	184 (24.1)	21.1 - 27.2
Diabetes	86 (11.3)	9.0 - 13.5
Epilepsy	9 (1.2)	0.4 - 1.9
Family history of DD	87 (11.4)	9.2 - 13.7
Hand injury ´	207 (27.1)	24.0-30.3
Manual labor	274 (35.9)	32.6-39.5
Ledderhose disease	11 (1.4)	0.6 - 2.3
Alcohol intake weekly, in us	nits	
None	263 (34.6)	31.2-38.0
1–5	218 (28.7)	25.5-31.9
6–10	138 (18.2)	15.4-20.9
11–15	77 (10.1)	8.0 - 12.3
16-20	28 (3.7)	2.3 - 5.0
>20	36 (4.7)	3.2-6.2
Dexterity	,	
Left	83 (10.9)	8.7-13.1
Right	666 (87.3)	84.9-89.7
Bimanual	14 (1.8)	0.9 - 2.8

IQR, interquartile range; DD, Dupuytren disease.

characteristics are listed in Table 1. There were no differences between the participants and nonresponders regarding sex, analyzed with the Pearson chi-square test (p = 0.635). The age of participants ranged from 50 to 89 years, with a median age of 62 years (interquartile range, 56 to 69 years). The nonresponse group had a median age of 64 years (interquartile range, 57 to 77 years) and was statistically significantly older than the group of

participants (Mann-Whitney U test, p < 0.001). Furthermore, nonresponse was not equally distributed over age categories (Pearson chi-square test, p < 0.001); in age categories younger than 70 years, more individuals were willing to participate than in the older categories. Comparison of percentages regarding smoking habits, alcohol consumption, and the presence of diabetes mellitus between our study population and the general population of The Netherlands¹⁵ showed that there were no explicit differences between these populations (Table 2).

In total, 169 participants were affected with Dupuytren disease, a prevalence of 22.1 percent (95 percent CI, 19.2 to 25.0 percent). Dupuytren disease was more common in men than in women, and prevalence increased with age (Table 3). The majority (n = 137) of the affected participants had palmar nodules without finger contractures (Iselin degree I). In 32 participants, a contracture of one or more digits was present, a prevalence of 17.9 percent for nodules and 4.2 percent for contractures in our population. Primary Dupuytren disease was confirmed in 162 patients, and recurrent disease was much rarer; this condition was seen in only seven patients. A total of 91 patients (53.8 percent) had bilateral disease. In primary disease, 119 left hands (15.6 percent) and 131 right hands (17.2 percent) were affected. Recurrent disease was noted in five left hands (0.7 percent) and in five right hands (0.7 percent). In total, 456 rays were affected, resulting in an average of 2.7 affected rays per patient. The majority (84.9 percent) of the 436 primary affected rays had palmar nodules without contracture (Iselin degree

Table 2. Prevalence of Three Study Parameters in the General Population of The Netherlands and Our Study Population

Risk Factor by Age		The Netherla	nds*		Study Population SE	ation
Category	%	SE	95% CI	%		95% CI
Smoking						
50–55 years	31.6	1.4	28.9-34.3	32.1	3.7	24.9-39.3
56–65 years	26.1	1	24.1-28.1	26.9	2.5	22.0 - 31.7
66–75 years	17.6	1.1	15.4–19.8	19.4	3.1	13.3-25.5
>75 years	10.5	1	8.5-12.5	12.4	3.0	6.5 - 18.3
Alcohol consumption (>20/wk)					
50–55 years	9.2	1.3	6.7 - 11.7	6.2	1.9	2.5 - 9.9
56–65 years	10.1	1	8.1-12.1	4.1	1.1	1.9 - 6.3
66–75 years	11.3	1.3	8.8-13.8	6.9	2.0	3.0 - 10.8
>75 years	5.5	1.1	3.3-7.7	1.7	1.2	-0.62 - 3.9
Diabetes						
50–55 years	5.1	0.7	3.7-8.0	3.7	1.5	0.8 - 6.6
56–65 years	8.0	0.6	6.8 - 14.0	11.6	1.8	8.1-15.1
66–75 years	15.5	1	13.5-27.5	10.6	2.4	5.9-15.4
>75 years	16.1	1.2	13.7 - 28.1	21.5	3.7	14.2-28.8

^{*}Data from the central bureau of statistics, Statistics Netherlands (Statline database. Available at: http://statline.cbs.nl. Accessed September 25, 2012).

Table 3. Prevalence in Different Age Categories

Total			Men			Women			
Age, yr	No.	DD+	DD%	No.	DD+	DD%	No.	DD+	DD%
50–55 years	162	8	4.9	72	4	5.6	90	4	4.4
56–60 years	174	22	12.6	78	11	14.1	96	11	11.5
61–65 years	146	29	19.9	66	15	22.7	80	14	17.5
66–70 years	99	28	28.3	49	15	30.6	50	13	26.0
71–75 years	61	24	39.3	29	12	41.4	32	12	37.5
76–80 years	57	30	52.6	24	18	75.0	33	12	36.4
81–85 years	31	16	51.6	14	8	57.1	17	8	47.1
86–90 years	33	12	36.4	16	9	56.3	17	3	17.6
Total	763	169	22.1	348	92	26.4	415	77	18.6

DD+, number with Dupuytren disease; DD%, percentage with Dupuytren disease.

I); only 49 rays (10.7 percent) had an Iselin score higher than degree I. Eight rays had been successfully operated on for Dupuytren disease, and in 20 rays recurrent disease was present (Fig. 2).

The difference in prevalence for the hands and fingers was tested with generalized estimating equations, excluding successfully operated rays. The results showed that there was no interaction effect between fingers and hands (p =0.59) and that the prevalence of Dupuytren disease at each ray was distributed equally between both hands (p = 0.21). However, a difference between fingers was detected (p < 0.001). The most frequently affected ray was the ring finger, followed by the middle finger and the little finger (Fig. 3). Pairwise comparison of differences between fingers showed that prevalence of all fingers differed significantly from each other, except for the prevalence of the middle finger and the little finger (p = 0.20).

Potential Risk Factors for Dupuytren Disease

The prevalence increased from 4.9 percent in participants aged 50 to 55 years to 52.6 percent among those aged 76 to 80 years (Table 3). The median age of participants with Dupuytren disease was higher compared with patients without the disease, 68 years (interquartile range, 62 to 77.5 years) and 59 years (interquartile range, 55 to 67 years), respectively (p < 0.001). Dupuytren disease was more common in men than in women; in total, 92 men and 77 women were affected, resulting in a prevalence of 26.4 percent in men and 18.6 percent in women (logistic regression adjusted for age categories: p = 0.007; OR, 1.67; 95 percent CI, 1.15 to 2.24). Other statistically significant risk factors for Dupuytren disease seen in our population were hand injury in the past, excessive alcohol consumption, familial occurrence of Dupuytren disease, and presence of Ledderhose disease (Table 4).

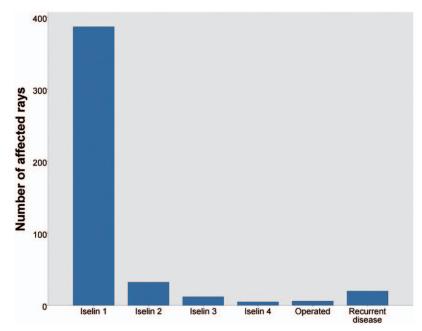


Fig. 2. Severity of disease.

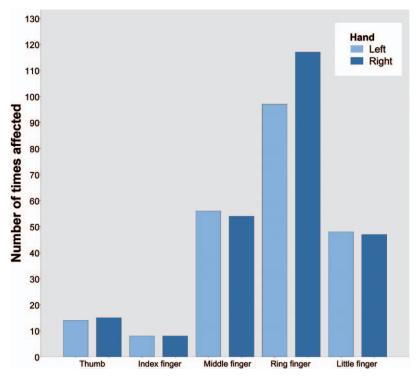


Fig. 3. Number of times a certain ray was affected with Dupuytren disease.

Prediction Model

The final analyses were conducted to determine a logistic prediction model for the prevalence of Dupuytren disease. Age was entered as both a linear and a quadratic effect. Table 5 shows the

coefficients of the final prediction model in the logit scale after applying backward elimination. This model can be used to estimate the prevalence of Dupuytren disease in men and women, depending on the presence of certain risk factors (Fig. 4).

Table 4. Potential Risk Factors among Patients with Dupuytren Disease and the Reference Cohort*

Risk Factors	Dupuytren Disease $(n = 169)$ (%)	Reference Cohort $(n = 594)$ (%)	Odds Ratio (95% CI)	p
Age category				<0.001†
50–55 years	8 (4.7)	154 (25.9)	1 (NA)	
56–60 years	22 (13.0)	152 (25.6)	2.87 (1.20–6.45)	
61–65 years	29 (17.2)	117 (19.7)	4.77 (2.10–10.82)	
66–70 years	28 (16.6)	71 (12.0)	7.59 (3.30–17.49)	
71–75 years	24 (14.2)	37 (6.2)	12.49 (5.20–30.01)	
76–80 years	30 (17.8)	27 (4.5)	21.39 (8.87–51.60)	
81–85 years	16 (9.5)	15 (2.5)	20.53 (7.55–55.85)	
86–90 years	12 (7.1)	21 (3.5)	11.00 (4.03–30.02)	
Male sex‡	92 (54.4)	256 (43.1)	1.67 (1.15–2.24)	0.007 †
Smoking§	30 (17.8)	154 (25.9)	0.83 (0.52–1.33)	0.43
Alcohol consumption§	21 (12.4)	43 (7.3)	2.37 (1.28–4.39)	0.006†
(>15 units/wk)	(**************************************	(111)	(*** *** **** **** **** **** **** **** ****	
Diabetes mellitus‡	27 (16.0)	59 (9.9)	1.17 (0.69–1.99)	0.56
Epilepsy‡	5 (3.0)	4(0.7)	4.03 (1.01–16.04)	0.05
Hand injury§	54 (32.1)	153 (25.8)	1.56 (1.04–2.35)	$0.03 \dagger$
Manual labor§	59 (35.1)	215 (36.3)	0.91 (0.62–1.34)	0.63
Family history‡	40 (23.7)	47 (7.9)	3.04 (1.83–5.05)	< 0.001 †
Ledderhose!	10 (5.9)	1(0.2)	39.36 (4.86–318.95)	0.001+
Knuckle pads§	31 (19.6)	85 (14.4)	1.48 (0.90–2.44)	0.12

NA, not applicable.

^{*}Missing values in patients with Dupuytren disease: hand injury, n = 1; manual labor, n = 1. Missing values in the reference cohort: alcohol consumption, n = 3; manual labor, n = 2.

[†]Statistically significant difference between participants with Dupuytren disease and reference cohort in logistic regression analysis.

[‡]Adjusted for age categories in logistic regression analysis.

[§]Adjusted for age categories and sex in logistic regression analysis.

Table 5. Logistic Prediction Model for Prevalence of Dupuytren Disease

Risk Factors	В	95% CI
Constant	-1.146	-1.4772 to -0.81476
Age	1.093	0.8183 to 1.3678
Age squared	-0.294	-0.4813 to -0.1075
Male sex	0.460	0.0676 to 0.8523
Alcohol consumption		
(≥15 units/week)	0.801	0.1459 to 1.4564
Family history	1.156	0.6337 to 1.6776
Ledderhose disease	3.489	1.4032 to 5.5738

The model was investigated for its goodness-of-fit by adding interactions between age and age squared and the other risk factors, but none of the interactions was significant (p > 0.175). This goodness-of-fit test was not conducted for Ledderhose disease, because there were too few events to fit a reliable quadratic model in age for each subgroup. Furthermore, the Hosmer-Lemeshow test did not

demonstrate a lack of fit of the prediction model (p = 0.274).

DISCUSSION

The purpose of this study was twofold: first, to investigate the prevalence of Dupuytren disease in the general population aged 50 years and older in The Netherlands; and second, to study the association between Dupuytren disease and potential risk factors. We conducted a cross-sectional study with a stratified random sample by age of 1360 individuals. In total, 763 eventually participated. Our study revealed a prevalence of 22.1 percent (95 percent CI, 19.2 to 25.0 percent). Men were more often affected than women, and the prevalence increased with age from 4.9 percent in age category 50 to 55 years up to 52.6 percent in participants between 76 and 80 years of age.

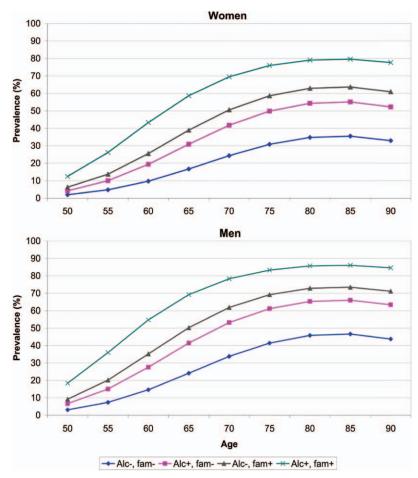


Fig. 4. Prevalence of Dupuytren disease in women and men. *Alc-*, consumption of less than 15 alcoholic units per week; *Alc+*, consumption of more than 15 alcoholic units per week; *fam-*, no family history of Dupuytren disease; *fam+*, first-degree relative with Dupuytren disease. Ledderhose disease was not included as a risk factor in this figure.

Our findings are in agreement with results from Zerajic and Finsen¹⁹ and Degreef and De Smet,²⁰ with prevalence rates of 25.4 and 31.6 percent, respectively, in the general population of men and women older than 50 years. The majority of our participants only had palmar nodules; contractures were rarely seen. This is in accordance with the findings of others. 19,20 Some authors who performed studies in a nonhospital environment have found lower prevalence rates, ranging from 5.6 to 13.5 percent. 4,9,21-23 There are several possible explanations for this variability in prevalence, such as regional differences, because most of these prior studies were performed in Scandinavia. Second, some of the studied populations seem to be much younger than our population.^{4,21,23} In the case of the 6 percent prevalence published by Bergenudd et al.,9 the difference may be explained by a difference in diagnostic criteria, because they examined the hands for "Dupuytren's contracture," whereas we included other features: tethered skin, nodules, cords, and contractures.

Another cause for variability in prevalence might be a difference in experience with Dupuytren disease between the investigators. In the literature, an article by Noble et al. is often cited as an example of a discrepancy in prevalence when a physician diagnoses the disease (18 percent) compared with a hand surgeon (42 percent).²⁴ It is frequently suggested that the physician may have missed Dupuytren disease. We think that such a conclusion is unjustified, because the disease was diagnosed in two different populations that did not have similar baseline characteristics. A Danish study carried out by a nurse and a medical student also found a low prevalence of 11 percent.⁴ However, a study in Bosnia, carried out by a junior clinician, reported a high rate of Dupuytren disease, suggesting that less experienced researchers may not underestimate prevalence.¹⁹ These discrepancies complicate interpreting the importance of experience in relation to the prevalence found, especially because the prevalence figures concern different countries.

The incidence of operative intervention and recurrent disease was low in our study population. It is difficult to compare these rates with the population at large, because data about the incidence of surgical procedures for Dupuytren disease in the general population are not readily available. Furthermore, the majority of prevalence studies investigated merely the prevalence of current Dupuytren disease and did not show data about intervention rates or recurrent disease in their

study population. In 1999, Rayan suggested that there are two types of Dupuytren disease, namely, typical Dupuytren disease and atypical Dupuytren disease. Patients with typical Dupuytren disease have progressive disease that often requires surgical intervention. In contrast, patients with atypical disease have a mild form of the disease that is usually located only in the palm of the hand. This form is nonprogressive, and treatment is rarely indicated.²⁵ The low incidence of surgical intervention in our study population might suggest that atypical Dupuytren disease is common in the general population.

A secondary goal of this study was to investigate the role of potential risk factors in the development of Dupuytren disease. In our population, a female-to-male ratio of 1:1.2 was found. It is interesting that in several studies aimed at treatment of Dupuytren disease, a different sex distribution was observed, ranging from 1:3.8 to 1:5. ^{26–28} This might suggest that the course of the disease is different in women and that treatment is less frequently performed in women than in men.

We know from previous studies that prevalence rises with age. This was supported by our results; prevalence increased strongly with rising age to a maximum prevalence of 52.6 percent. However, in the highest age categories, a downward trend in prevalence was seen. Because of our age stratification, we believe this to be a reliable result. This finding is in agreement with some indications that patients with Dupuytren disease might have an increased mortality rate. ^{29–31} In contrast, in some studies, prevalence rates continued to rise with age. ^{10,19,20,32–35} Therefore, the implications of this finding are difficult to interpret.

In the multivariable analyses, we adjusted for age categories because we stratified age into eight categories. In addition, in some analyses, we also adjusted for sex, as this might have been a confounder in certain variables, such as smoking and alcohol consumption.

In our population, there was no association between Dupuytren disease and diabetes in the multivariable analysis corrected for age and sex. This was in agreement with results from other studies. ^{1,10,19,36} Some other researchers did find a significant difference in prevalence between patients with diabetes and their control group, ^{37–41} but it is not clear whether this effect was adjusted for age.

Several authors have tried to elucidate the association between Dupuytren disease and diabetes. An explanation for this association might be that microvascular changes in diabetes result

in local hypoxia. This hypoxia may induce the activation of several cellular pathways, eventually resulting in formation of fibromatous tissue. 42,43 However, as mentioned, the results on this topic are contradictory.

Smoking has been associated with Dupuytren disease. 10,35,44 It is well known that smoking affects the peripheral circulation; this could result in peripheral hypoxia as mentioned before, and may explain the association between smoking and Dupuytren disease. Our findings, however, do not support this hypothesis, because smoking was not a risk factor in our population, nor was smoking identified as a risk factor in several other studies. 9,19,45 Other previously associated risk factors that could not be linked to Dupuytren disease in our population are epilepsy and manual labor.

The following risk factors for Dupuytren disease were statistically significant in our multivariable analysis: age, male sex, hand injury in the past, excessive alcohol consumption, family history of Dupuytren disease, and presence of Ledderhose disease. After backward elimination, we have been able to determine a logistic prediction model for the prevalence of Dupuytren disease with all of these risk factors except hand injury in the past. This model can be used to estimate the prevalence in men and women, depending on the presence of the above-mentioned risk factors. Most parameter estimates of risk factors incorporated into the final model have a small confidence interval, but the confidence interval of Ledderhose disease is very broad because of the small number of events. Therefore, we considered the outcome of this potential risk factor less reliable and did not include this variable in the figures of our prediction model.

One of the strengths of this study was our sampling method. Because we drew a random sample stratified by age, we were able to include enough participants in each age category. Furthermore, we visited potential participants at home, which increased the willingness to participate. Nonetheless, we did not entirely reach the number of desired participants. The proportion of nonresponders was not equally distributed across age categories, and nonresponders were significantly older than the participants. This may have resulted in an underestimation of the prevalence of Dupuytren disease. Indeed, a weighted analysis, where the weights were selected to make the sample size in the same ratio with the population sizes, resulted in a prevalence of 23.7 percent. This is close to our result of 22.1 percent, so the imbalance in nonresponse across age categories apparently had a minimal effect on our estimate. Another strength of our study is that we compared our results with available data from the central bureau of statistics (Statistics Netherlands). Because there were no explicit differences in outcome, it can be assumed that our study population accurately represents the general population in The Netherlands.

This study shows that Dupuytren disease—particularly, the nodular form—is common among citizens of The Netherlands aged 50 years and older. Dupuytren disease is highly age dependent, and is more frequently seen in men than in women. A logistic prediction model was developed to estimate the prevalence of Dupuytren disease based on the presence of the significant risk factors sex, age, alcohol consumption, presence of Ledderhose disease, and a positive family history of Dupuytren disease.

Rosame Lanting, M.D.

Department of Plastic Surgery
University Medical Center Groningen
HPC BB81
P.O. Box 30.001
9700 RB Groningen, The Netherlands
r.lanting@umcg.nl

ACKNOWLEDGMENT

This research was funded by the University Medical Center Groningen.

REFERENCES

- 1. Eadington DW, Patrick AW, Frier BM. Association between connective tissue changes and smoking habit in type 2 diabetes and in non-diabetic humans. *Diabetes Res Clin Pract.* 1991;11:121–125.
- 2. Arafa M, Noble J, Royle SG, Trail IA, Allen J. Dupuytren's and epilepsy revisited. *J Hand Surg Br.* 1992;17:221–224.
- 3. Geoghegan JM, Forbes J, Clark DI, Smith C, Hubbard R. Dupuytren's disease risk factors. *J Hand Surg Br.* 2004;29:423–426.
- 4. Godtfredsen NS, Lucht H, Prescott E, Sørensen TI, Grønbaek M. A prospective study linked both alcohol and tobacco to Dupuytren's disease. *J Clin Epidemiol.* 2004;57:858–863.
- 5. Burge P. Genetics of Dupuytren's disease. *Hand Clin.* 1999;15:63–71.
- 6. Hu FZ, Nystrom A, Ahmed A, et al. Mapping of an autosomal dominant gene for Dupuytren's contracture to chromosome 16q in a Swedish family. *Clin Genet*. 2005;68:424–429.
- Hindocha S, John S, Stanley JK, Watson SJ, Bayat A. The heritability of Dupuytren's disease: Familial aggregation and its clinical significance. *J Hand Surg Am.* 2006;31:204–210.
- 8. Dolmans GH, Werker PM, Hennies HC, et al.; Dutch Dupuytren Study Group; German Dupuytren Study Group; LifeLines Cohort Study; BSSH-GODD Consortium. Wnt signaling and Dupuytren's disease. N Engl J Med. 2011;365:307–317.

- Bergenudd H, Lindgärde F, Nilsson BE. Prevalence of Dupuytren's contracture and its correlation with degenerative changes of the hands and feet and with criteria of general health. J Hand Surg Br. 1993;18:254–257.
- Gudmundsson KG, Arngrímsson R, Sigfússon N, Björnsson A, Jónsson T. Epidemiology of Dupuytren's disease: Clinical, serological, and social assessment. The Reykjavik Study. *J Clin Epidemiol.* 2000;53:291–296.
- 11. Mitra A, Goldstein RY. Dupuytren's contracture in the black population: A review. *Ann Plast Surg.* 1994;32:619–622.
- Slattery D. Review: Dupuytren's disease in Asia and the migration theory of Dupuytren's disease. ANZ J Surg. 2010;80:495–499.
- Hindocha S, McGrouther DA, Bayat A. Epidemiological evaluation of Dupuytren's disease incidence and prevalence rates in relation to etiology. *Hand (NY)* 2009;4:256–269.
- 14. Duin van C, Garssen J. Population forecast 2010–2060: An aging population and increased life expectancy (Bevolkingstrend 2010–2060: Sterkere vergrijzing en een langere levensduur). Available at: http://www.cbs.nl. Accessed February 24, 2012.
- 15. Statline database. Available at: http://statline.cbs.nl. Accessed September 25, 2012.
- 16. Iselin M, Iselin F. Maladie de Dupuytren. In: *Traité de chirugie de la main*. Brussels: Flammarion; 1967:676–678.
- 17. Daniel WW. Biostatistics: A Foundation for Analysis in the Health Sciences. 7th ed. New York: Wiley; 1999:180–185, 268–270.
- Statistical Yearbook 2010 of Groningen City Council. Available at: http://www.os-groningen.nl/images/stories/rapport/Statistisch_Jaarboek_2010.pdf. Accessed August 14, 2011.
- Zerajic D, Finsen V. Dupuytren's disease in Bosnia and Herzegovina: An epidemiological study. BMC Musculoskelet Disord. 2004;5:10.
- 20. Degreef I, De Smet L. A high prevalence of Dupuytren's disease in Flanders. *Acta Orthop Belg.* 2010;76:316–320.
- 21. Beighton P, Valkenburg HA. Bone and joint disorders on Tristan da Cunha. *S Afr Med J.* 1974;48:743–747.
- 22. Finsen V, Dalen H, Nesheim J. The prevalence of Dupuytren's disease among 2 different ethnic groups in northern Norway. *J Hand Surg Am.* 2002;27:115–117.
- Mikkelsen OA. The prevalence of Dupuytren's disease in Norway: A study in a representative population sample of the municipality of Haugesund. *Acta Chir Scand*. 1972;138:695–700.
- 24. Noble J, Heathcote JG, Cohen H. Diabetes mellitus in the aetiology of Dupuytren's disease. *J Bone Joint Surg Br.* 1984;66:322–325.
- Rayan GM. Clinical presentation and types of Dupuytren's disease. *Hand Clin*. 1999;15:87–96, vii.
- Hurst LC, Badalamente MA, Hentz VR, et al.; CORD I Study Group. Injectable collagenase clostridium histolyticum for Dupuytren's contracture. N Engl J Med. 2009;361:968–979.
- Pess GM, Pess RM, Pess RA. Results of needle aponeurotomy for Dupuytren contracture in over 1,000 fingers. *J Hand Surg Am.* 2012;37:651–656.
- van Rijssen AL, Gerbrandy FS, Ter Linden H, Klip H, Werker PM. A comparison of the direct outcomes of percutaneous

- needle fasciotomy and limited fasciectomy for Dupuytren's disease: A 6-week follow-up study. J Hand Surg Am. 2006;31:717–725.
- Gudmundsson KG, Arngrímsson R, Sigfússon N, Jónsson T. Increased total mortality and cancer mortality in men with Dupuytren's disease: A 15-year follow-up study. J Clin Epidemiol. 2002;55:5–10.
- Mikkelsen OA, Høyeraal HM, Sandvik L. Increased mortality in Dupuytren's disease. J Hand Surg Br. 1999;24:515–518.
- 31. Wilbrand S, Ekbom A, Gerdin B. A cohort study linked increased mortality in patients treated surgically for Dupuytren's contracture. *J Clin Epidemiol.* 2005;58:68–74.
- 32. Su CK, Patek AJ Jr. Dupuytren's contracture: Its association with alcoholism and cirrhosis. *Arch Intern Med.* 1970;126:278–281.
- 33. Arafa M, Steingold RF, Noble J. The incidence of Dupuytren's disease in patients with rheumatoid arthritis. *J Hand Surg Br.* 1984;9:165–166.
- 34. Guğmundsson KG, Arngrímsson R, Sigfússon N, Jónsson T. Prevalence of joint complaints amongst individuals with Dupuytren's disease: From the Reykjavík study. Scand J Rheumatol. 1999;28:300–304.
- 35. Burke FD, Proud G, Lawson IJ, McGeoch KL, Miles JN. An assessment of the effects of exposure to vibration, smoking, alcohol and diabetes on the prevalence of Dupuytren's disease in 97,537 miners. *J Hand Surg Eur Vol.* 2007;32:400–406.
- 36. Bridgman JF. Periarthritis of the shoulder and diabetes mellitus. *Ann Rheum Dis.* 1972;31:69–71.
- 37. Eadington DW, Patrick AW, Collier A, Frier BM. Limited joint mobility, Dupuytren's contracture and retinopathy in type 1 diabetes: Association with cigarette smoking. *Diabet Med.* 1989;6:152–157.
- 38. Chammas M, Bousquet P, Renard E, Poirier JL, Jaffiol C, Allieu Y. Dupuytren's disease, carpal tunnel syndrome, trigger finger, and diabetes mellitus. *J Hand Surg Am*. 1995;20:109–114.
- 39. Ardic F, Soyupek F, Kahraman Y, Yorgancioglu R. The musculoskeletal complications seen in type II diabetics: Predominance of hand involvement. *Clin Rheumatol.* 2003;22:229–233.
- 40. Akyol A, Kiylioglu N, Copcu E, Guney E, Aydeniz A. Is diabetes mellitus type 2 a risk factor for Dupuytren's contracture in the Mediterranean region? *Plast Reconstr Surg.* 2006;117:2105–2106.
- 41. Savaş S, Köroğlu BK, Koyuncuoğlu HR, Uzar E, Celik H, Tamer NM. The effects of the diabetes related soft tissue hand lesions and the reduced hand strength on functional disability of hand in type 2 diabetic patients. *Diabetes Res Clin Pract.* 2007;77:77–83.
- 42. Kischer CW, Speer DP. Microvascular changes in Dupuytren's contracture. *J Hand Surg Am.* 1984;9:58–62.
- 43. Badalamente MA, Hurst LC, Grandia SK, Sampson SP. Platelet-derived growth factor in Dupuytren's disease. *J Hand Surg Am.* 1992;17:317–323.
- 44. Burge P, Hoy G, Regan P, Milne R. Smoking, alcohol and the risk of Dupuytren's contracture. *J Bone Joint Surg Br.* 1997;79:206–210.
- 45. Mackenney RP. A population study of Dupuytren's contracture. *Hand* 1983;15:155–161.