Phenotype of Dupuytren disease

Patterns of combination of affected fingers in relation to severity of the disease

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Abstract

INTRODUCTION
Dupuytren disease is a fibroproliferative condition affecting the palmar fascias of the hand and fingers characterized by a variable expression and an unpredictable course. Little is known about patterns of the disease and if certain combinations occur only in severe disease. The aim of our study was to try to identify such patterns. We hypothesized that there is a relation between the affected rays and the severity of the disease, whereby the fourth and fifth digit are most frequently affected and that an affected thumb or first web space is associated with a severe contracture of fourth and fifth finger.

METHODS
Photographs and measured extension deficits of 531 hands were studied and each ray was assessed according to the classification of Iselin. Frequency tests were performed to see if certain combinations of Dupuytren affected rays occurred more often than others. Fisher’s exact test was performed to study the association between severe contractures of ring and little finger and an affected radial side. A multivariate logistic regression was performed to adjust for possible confounders.

RESULTS
We found 25 different patterns of affected rays. Most frequently presented patterns were: an affected ring and little finger, an affected middle, ring and little finger and an affected middle and ring finger. Univariate analysis showed a significant association between radial involvement and a severe contracture of ring and little finger. In multivariate analysis this significance disappeared. Furthermore, we found an association between alcohol consumption, radial side involvement and a severe contracture of ring and little finger.

CONCLUSION
This study gives an overview of patterns in Dupuytren disease, and shows in particular that excessive alcohol use has a possible influence on a severe contracture of ring and little finger, especially in patients with an affected thumb.
Samenvatting

INTRODUCTIE
Morbis Dupuytren is een fibroproliferatieve aandoening waarbij de palmaire fascia van de hand en vingers wordt aangetast en wordt gekenmerkt door een variatie in expressie en een onvoorspelbaar beloop. Er is weinig bekend over patronen in de ziekte en of bepaalde combinaties alleen optreden bij een ernstigere ziekte. Onze hypothese is dat er een relatie bestaat tussen de aangedane stralen en de ernst van de ziekte, waarbij de ringvinger en pink het meest frequent zijn aangedaan en dat een aangedane duim en eerste webspace geassocieerd wordt met een ernstige contractuur van ringvinger en pink.

METHODEN
Foto’s en gemeten extensie beperkingen van 531 handen werden bestudeerd en elke straal werd beoordeeld volgens de classificatie van Iselin. Frequentie testen werden uitgevoerd om te onderzoeken of bepaalde combinaties van aangedane stralen door de ziekte van Dupuytren vaker voorkwamen dan andere. Fisher’s exact test werd uitgevoerd om de associatie tussen een ernstige contractuur van ringvinger en pink en een aangedane radiale zijde van de hand te bestuderen. Een multivariate logistische regressie analyse werd uitgevoerd om te corrigeren voor mogelijke confounders.

RESULTATEN
Wij vonden 25 verschillende patronen van aangedane stralen. De meest voorkomende patronen waren: een aangedane ringvinger en pink, een aangedane middelvinger, ringvinger en pink en een aangedane middelvinger en ringvinger. Univariate analyse liet een significante associatie zien tussen een aangedane radiale zijde en een ernstige contractuur van ringvinger en pink. In de multivariate analyse bleef deze associatie niet significant. Daarnaast zagen we een associatie tussen alcohol consumptie, een aangedane radiale zijde en een ernstige contractuur van ringvinger en pink.

CONCLUSIE
Deze studie geeft een overzicht van mogelijke patronen in de ziekte van Dupuytren, en laat in het bijzonder zien dat overmatig alcoholgebruik mogelijk van invloed is op een ernstige contractuur van ringvinger en pink, in het bijzonder bij patiënten met een aangedane radiale zijde.
Introduction

Dupuytren disease is a benign fibromatosis of the palmer fascia of the hand and fingers. It is a condition that usually starts with painless thickening in the palm, known as noduli. Subsequently cord-like structures may develop, connecting the noduli and leading to flexion contractures of the fingers. The disease was named after Baron Guillaume Dupuytren in 1831 (1), but it was already described by the Swiss physician Felix Plater in 1614 (2).

1.1 Prevalence and Associated diseases
The prevalence of Dupuytren disease in different geographical locations has been reported to range between 0.2% and 56% (3). This variation may be due to either genetic factors, environmental factors or a combination of both. However, it is not unlikely that the variation is caused by differences in study design or inclusion criteria, such as age and co-morbidity. The highest prevalence can be found in Northern European countries, like Scandinavia and the United Kingdom, where the majority of the prevalence studies have been performed (3). Also in Australia and North America a high prevalence of Dupuytren disease has been found (4,5), whereas in Africa and Asia sporadic cases of Dupuytren disease have been reported (6,7). Until now, little is known about the prevalence of Dupuytren disease in the Netherlands (8). The prevalence of Dupuytren disease increases with age and men are more affected than women. By the ninth decade of life however, the incidence in women is as high as in men (9,10).

Furthermore, Dupuytren disease is associated with ectopic lesions such as Garrod’s knuckle pads, a fibromatosis on the dorsal side of the proximal interphalangeal joint, Ledderhose disease, a fibromatosis of the plantar fascia of the foot, and Peyronie’s disease, a fibromatosis of the dorsal surface of the penis.

1.2 Pathogenesis
The pathogenesis of Dupuytren disease has not yet been completely elucidated. Recently nine chromosomal loci associated with susceptibility to Dupuytren disease have been identified by the Departments of Plastic Surgery and Genetics of the University Medical Center Groningen (UMCG) (11), but the aetiology entails a more complex process. Diseases like diabetes mellitus and environmental factors like cigarette smoking, alcohol abuse, alcohol-induced liver disease, trauma and manual labour have been postulated to contribute to developing Dupuytren disease (12-16). These studies however, have reported inconsistent results and some studies have not found an etiologic contribution of these risk factors (4,17). Therefore these risk factors remain controversial.
1.3 Dissection studies
To obtain more knowledge about the course of Dupuytren disease, much research has been directed to anatomical dissection studies. In 1974 McFarlane tried to find patterns in affected fascia (18). From this study he concluded that a metacarpophalangeal (MCP) joint contracture can only be caused by a pretendinous cord. A proximal interphalangeal (PIP) joint contracture however, can be the result of a central cord, which in fact often is an extension of the pretendinous cord, a lateral digital sheet cord, formed from the fascia between the skin and the neurovascular bundle at either or both sides of the finger and a spiral cord, formed from the affected fibres surrounding the neurovascular bundle (Figure 1).

Figure 1: (left) Normal anatomy of parts of the palmar and digital fascia that can become involved in Dupuytren disease. (center) A central cord as an extension of the pretendinous cord. (right) A lateral cord and a spiral cord (18).
Dupuytren disease of the thumb was first described in 1833 by Guérin (19). Tubiana and De Frenne et al identified four fibrous structures from the palm to the thumb with the tendency to become involved in Dupuytren disease (Figure 2). These authors saw that the cords A, C and D as described in Figure 4 were responsible for thumb contractures, limiting thumb movement in palmar and/or radial abduction. The radial longitudinal fibres, which are the equivalent of a pretendinous band, may – once affected – limit extension in MCP and/or IPJ.

Figure 2: Location of pathological fibrous formation on the radial side of the hand. A, the thenar muscle fascia; B, the radial longitudinal fibres of the palmar aponeurosis; C, the distal transverse commissural ligament of the first web; D, the proximal transverse commissural ligament of the first web (19).
1.4 Diagnosis and Phenotype

The diagnosis Dupuytren disease can easily be made in most cases, although small skin irregularities in the beginning of the disease can be confused with other diseases or missed. The disease usually starts with painless nodules in the palm, firm masses located on the superficial aspect of the pretendinous bands of the palmar fascia or on the palmar aspect of the fingers at the proximal phalanx. Skin pitting is often the first sign of a contracture. Cord like structures may appear over months or years, slowly causing flexion contractures of the metacarpophalangeal (MCP) joint and/or proximal interphalangeal (PIP) joint (Figure 3) (20). The distal interphalangeal (DIP) joint is seldom involved and flexion contractures of the DIP joints are rarely seen. However, a severe contracture of the MCP and the PIP joints may give rise to a compensatory hyperextension of the DIP joint, also known as a Boutonnière deformity, especially in recurrent cases.

Stage 1
The condition generally starts as a small lump in the palm of the hand usually just under the digit on the palmar crease

Stage 2
The disease spreads up the fascia and into the fingers

Stage 3
As it spreads up the fingers it eventually creates a tight cord which causes the fingers to bend and unable to straighten.

Figure 3: Illustration of clinical presentation in Dupuytren's disease (20).

The presentation and course of Dupuytren disease is variable and it is unknown why some patients develop minimal contractures over decades while others are saddled with severe disease in a shorter period of time. The disease is not restricted to different compartments of the hand and can extend to all fingers. Dupuytren disease often occurs bilateral, although not symmetrically, nor in the same phase. The ring finger and little finger are predominantly affected whereas the radial aspect of the hand is less often involved (21).

Most patients develop contractures gradually and they have hardly any impairment, before fingers have become severely bent. Then impaired hand and finger function occurs leading to difficulty with manual labour, putting on gloves, shake hands, washing and dressing, possibly leading to dependence on others.
1.5 Grading systems

In order to assess the severity of the disease, several grading systems have been developed over the years. In 1936 Meyerding developed a system to assess the degree of deformity and divided the severity of the disease into five categories (Table 1) (21). An important shortcoming of Meyerding’s classification is that the categories are related to the whole hand and little nuances in severity can be made, since it does not discriminate between for instance a contracture of 45° of four fingers and a contracture of one finger of 5°. Both deficits are scored as a grade I. Furthermore, grade IV is a subjective class without an absolute cutoff.

Table 1: Meyerding’s classification of Dupuytren disease (21)

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>Unnatural thickening of the palmar fascia and wrinkling of the skin, no contracture of a finger.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Definite contracture of one finger, but ≤ 60° of flexion in any joint</td>
</tr>
<tr>
<td>Grade II</td>
<td>Involvement of at least one finger with extension deficit ≥ 60°</td>
</tr>
<tr>
<td>Grade III</td>
<td>Indicates contracture of ≥ 2 fingers and contracture of ≥ 90° of one finger</td>
</tr>
<tr>
<td>Grade IV</td>
<td>More or less contracture of all the digits, the hand cannot be opened or the thumb fully extended</td>
</tr>
</tbody>
</table>

Iselin on the other hand utilized a more simple classification system, without the necessity to perform any measurements and he developed in 1965 a system to assess the severity of Dupuytren disease by visible contractures by joints (Table 2) (22).

Table 2: Iselin’s classification of Dupuytren disease (22)

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Palmar nodules and small cords without signs of contracture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II</td>
<td>Contracture of the metacarpophalangeal (MCP) joint</td>
</tr>
<tr>
<td>Stage III</td>
<td>Contracture of the MCP and proximal interphalangeal (PIP) joint</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Severe contracture of the MCP and the PIP joints with hyperextension of the distal interphalangeal (DIP) joint, also known as a Boutonnière deformity</td>
</tr>
</tbody>
</table>
In 1961 Tubiana et al developed a classification which was refined by Tubiana in 1986 and is still widely used (Figure 4) (23-25). According to this method staging is based on the total extension loss of all joints of each finger ray.

Although until now Tubiana’s classification is predominantly used, Abe criticized this grading system, because of the complexity and because both the MCP and PIP joints are included in one measurement. Having both joints in one measurement may misrepresent the state of disease, since involvement of the PIP joint can be associated with a more severe condition (26). Therefore Abe came up with a new grading system, making sure that each finger ray is evaluated with attention to proximal interphalangeal joint involvement (Table 3) (27).

Table 3: Abe’s classification of Dupuytren disease (27).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Involvement of the MCP joint only</td>
</tr>
<tr>
<td>II</td>
<td>Involvement of the PIP joint with extension lost &lt; 30°</td>
</tr>
<tr>
<td>III</td>
<td>Involvement of the PIP joint with extension loss between 30° - 60°</td>
</tr>
<tr>
<td>IV</td>
<td>Involvement of PIP joint with extension loss &gt; 60°</td>
</tr>
<tr>
<td>Status hand</td>
<td>Expressed by the grade of the worst affected finger</td>
</tr>
</tbody>
</table>

Figure 4: Tubiana’s classification of Dupuytren’s disease (24).
Nevertheless, none of these grading systems can correctly describe the severity of Dupuytren disease or predict surgical outcome, since the condition is characterized by a variable presentation in each individual and an unpredictable course.

1.6 Dupuytren’s diathesis
In 1963 Hueston noticed that certain patient characteristics were associated with a more aggressive type of Dupuytren disease and a higher tendency towards recurrences (28). He coined the term Dupuytren diathesis, characterized by an early onset of the disease, bilateral involvement, a positive family history and ectopic lesions including Garrod’s knuckle pads, penile fibromatosis (Peyronie’s disease) and plantar fibromatosis (Ledderhose disease). McFarlane confirmed the idea of Dupuytren’s diathesis with a large multicenter study in 1985 (18,29). However, the influence of each individual factor on recurrence and extension has never been determined. In 2004 Abe studied the diathesis’ characteristics in a Japanese cohort and found that ‘family history’ was not significantly associated with recurrence or extension of the disease (28). However, he identified ‘little finger surgery’ and ‘radial involvement’ as new risk factors and concluded, based on odds ratios, that plantar fibrosis, knuckle pads, and radial side involvement had more influence on recurrence and extension than bilateral hand involvement, little finger surgery, or an early onset of the disease. In 2006 Hindocha revisited the original diathesis features of ‘family history’, ‘bilateral involvement’ and ectopic lesions’ (30). He specified ‘family history’ to ‘family history with one or more siblings/parents’, ‘ectopic lesions’ to ‘Garrod’s knuckle pads’ and ‘early onset of the disease’ to ‘age at onset younger than 50 years’. Furthermore, he added ‘male gender’ to the diathesis features. In contrast to Abe’s results in 2004, Hindocha did not find an influence of radial side involvement on recurrence and extension.

1.7 Patterns
Dupuytren disease of the radial side, i.e. the index finger, first web space and thumb, received little attention over the years and was considered to be rare (21). Yet, the reported incidence varies from 8% to 63% (23,31,32). The ulnar side, however, is predominantly involved in Dupuytren disease and the ring finger is most frequently affected, followed by the little finger and the middle finger.

In 1935 Meyerding noticed certain combinations of affected fingers. He saw that the combination of an affected fourth and fifth finger most often occurred, followed by the combination of an affected third, fourth en fifth digit.

Tubiana declared in 1982 that restricted radial side involvement in Dupuytren disease rarely appeared and that radial involvement in most cases was associated with an affected ulnar side (23). He distinguished between three different types of radial involvement. (1) A mild form, with as feature a late onset by an already existing ulnar disease in the elderly patient. This type is responsible for minimal contractures and surgery is seldom necessary. (2) An average form, starting at a younger age then the previous form. This type can cause contractures which might need surgical intervention and is more diffuse present in both hands. (3) A malign form, which arises at a young age and in an early stage of the disease. This type is almost always accompanied by ulnar contractures and can take an aggressive course. Study subjects with these three different types of radial involvement answered largely to Dupuytren diathesis.

However, Milner et al. found in 2003 that patients with an affected thumb were on average eight years older and suffered on average five years longer from Dupuytren disease (33). They suggested that an affected radial side was not related to diathesis features. But, patients in their study with severe contractures of their thumb and first web space suffered from ulnar disease which required repeatedly surgery, suggesting an intractable form of disease.
1.8 Aim of this study, research question and hypothesis

Until now, little is known about exact patterns of the disease and if certain combinations occur only in severe disease.

In 2007 the Department of Plastic Surgery and Genetics of the UMCG started the Genetic Origin of Dupuytrens Disease and Associated Fibromatosis (GODDAF) study, a genomewide association study, in order to identify genes associated with Dupuytren disease. For this study patients were recruited from the outpatient clinics of the plastic surgery departments of six hospitals in the Netherlands, i.e. the UMCG, the Martini Hospital Groningen (MHG), the Isala Clinic Zwolle (ICZ), Medical Spectrum Twente (MST), Medical Center Leeuwarden (MCL) and the Catherina Hospital Eindhoven (CHE). In the outpatient clinics, plastic surgeons filled in a form which contained measured extension deficits using a goniometer and patients were asked to fill in a questionnaire and to provide blood samples and written informed consent. The medical photographer took preoperative digital photographs of both hands in all directions.

Thank to this study we have an enormous amount of data of an unique population. The aim of the present study was to research the phenotype of Dupuytren disease, by assessing photographs of Dupuytren affected hands using the classification of Iselin. This would be our first step to be able to link phenotype and genotype in the future, to increase knowledge about disease progress in order to optimize patient specific information about the expected course of Dupuytren disease. It might even influence the choice of treatment.

Our research question is: can patterns be recognized of the combination of affected rays and the severity of Dupuytren disease in relation to the affected rays, quantified according to the classification of Iselin, using preoperative digital photographs and goniometry data, in patients with Dupuytren disease from the GODDAF-population between 2007 and 2011 from the UMCG, MHG, MCL, ICZ, MST and CHE?

We hypothesized that there is a relation between the affected rays and the severity of the disease, whereby the fourth and fifth digit are most frequently affected and that an affected thumb and first webspace is associated with a severe contracture of fourth and fifth finger.
2. Methods

2.1 Participants
In this cross-sectional study, we used data of 1519 patients with Dupuytren disease, Peyronie’s disease and/or Ledderhose disease that were recruited between 2007 and 2011 from the outpatient clinics of the plastic surgery departments of six hospitals in the Netherlands, for the purpose of the Genetic Origin of Dupuytrens disease and Associated Fibromatosis (GODDAF) study. In our study only data from participants with primary Dupuytren disease who were seen by a plastic surgeon were used (Figure 5). Patients with isolated Ledderhose or Peyronie’s disease, patients whom had not primarily been studied by a plastic surgeon, but by students as part of pedigree analyses, and patients with recurrence of Dupuytren disease were excluded. Data that we used included a questionnaire filled in by the patient, preoperative digital photographs, taken by a medical photographer and measurements of contractures, made by a plastic surgeon using a goniometer.

Figure 5: Included patients. LD = Ledderhose disease. PD = Peyronie’s disease.
Phenotype of Dupuytren’s disease

Preoperative digital photographs were assessed and each ray was scored according to a modified classification of Iselin (Table 4). In this modified classification a flexion contracture of the PIP joint without involvement of the MCP joint was also scored as an Iselin stage III and a flexion contracture of the DIP joint, instead of a hyperextension, was also scored as an Iselin stage IV.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Palmar nodules and small cords without signs of contracture</td>
</tr>
<tr>
<td>II</td>
<td>Contracture of the metacarpophalangeal (MCP) joint</td>
</tr>
<tr>
<td>III</td>
<td>Contracture of the MCP joint and/or proximal interphalangeal (PIP) joint</td>
</tr>
<tr>
<td>IV</td>
<td>Contracture of the MCP joint and/or the PIP joints with hyperextension of the distal interphalangeal (DIP) joint or contracture of the DIP joint</td>
</tr>
</tbody>
</table>

We used both photographs and outcome of goniometry to come to a final grade. Each ray was assessed separately and subsequently all grades were combined into a five digit endcode for the whole the hand, starting with the thumb and ending with the little finger (Figure 6). Of the 1201 hands that qualified for analyses, 531 hands were included since of these both photographs and goniometry results were available (Figure 7).

Figure 6: Examples of the scoring system. A: Frontal view of a left hand. Digit IV is affected and the contracture involves the MCP and PIP joint. A skin pit is seen in digit V at the PIP joint. No other skin irregularities as skin pits or noduli are seen. The measured extension deficit is 15° over the MCP joint and 20° over the PIP joint of digit IV. The endcode of this hand is 00031. B: Side view of a left hand. A cord and skin irregularities are seen in the fourth ray, yet there is no extension deficit. The endcode of this hand is 00010.
Figure 7: From 1201 hands to 531 hands in total.
2.2 Statistical analyses
Statistical analyses were performed using SPSS inc. PASW statistics 20 (IBM corporation, Chicago, IL, USA).

2.2.1. Reliability of scoring method
To investigate the reliability of the modified Iselin scoring method, 531 hands were twice assessed by the main investigator (NK) to test intra-rater variability. In total 189 of these hands were additional assessed by a second investigator (RL) to test inter-rater variability. The agreement was measured with a linear weighted kappa, using MedCalc Software 12.

2.2.2. Prevalence of patterns
We performed frequency tests to investigate how often rays were individually affected and if certain combinations of Dupuytren affected rays occurred more than others. We presented data in a binary fashion, as ‘not affected’ and ‘affected’, i.e. noduli, skin pits and contractures of all categories.

The group of patients with an affected thumb was highlighted. For this group we also performed frequency tests to investigate certain combinations of Dupuytren affected rays in binary fashion, and we performed frequency tests to investigate how often an affected thumb was isolated affected and associated with other affected rays and how often an affected thumb was associated with contractures of other rays of all Iselin categories.

2.2.3. Affected thumb and contractures of digit four and five
In order to be able to address our aim, we divided our population in two groups: (1) patients without radial side involvement (n = 461); (2) patients with an affected radial side of the hand, i.e. thumb, first webspace and/or index finger (n = 70). We compared patient characteristics and risk factors between both groups using an Independent samples t-test for age, a Mann Whitney U test for duration of the disease and Pearson’s $\chi^2$ tests for the remaining variables. We performed Fisher’s exact tests to investigate if severe contractures of digit four and five were associated with an affected radial side, using Iselin’s classification. Contractures were considered mild in Iselin category II and severe in Iselin category III and IV. With a multivariate logistic regression we investigated possible confounders and we adjusted for risk factors of Dupuytren disease which were found significantly different between both groups. After multivariate analysis, significant factors or confounders were more thoroughly studied in case of a possible mediator model. Significance was set on $P < 0.05$. 


3. Results

3.1 Reliability of scoring method
Agreement between the two investigators (NK and RL) regarding the assessment of five rays ranged from 0.84 to 0.96, with an average score of 0.90 (Table 5). The agreement between the first assessment and the second assessment (NK) of the same photographs and measurements, ranged from 0.92 to 0.96 with an average score of 0.94 (Table 6).

<table>
<thead>
<tr>
<th>Digit</th>
<th>Weighted kappa</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>0.84</td>
<td>0.71 – 0.97</td>
</tr>
<tr>
<td>II</td>
<td>0.96</td>
<td>0.89 – 1.00</td>
</tr>
<tr>
<td>III</td>
<td>0.89</td>
<td>0.82 – 0.95</td>
</tr>
<tr>
<td>IV</td>
<td>0.90</td>
<td>0.85 – 0.95</td>
</tr>
<tr>
<td>V</td>
<td>0.90</td>
<td>0.85 – 0.94</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Digit</th>
<th>Weighted kappa</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.93</td>
<td>0.87 – 0.98</td>
</tr>
<tr>
<td>II</td>
<td>0.93</td>
<td>0.88 – 0.99</td>
</tr>
<tr>
<td>III</td>
<td>0.92</td>
<td>0.89 – 0.96</td>
</tr>
<tr>
<td>IV</td>
<td>0.94</td>
<td>0.92 – 0.96</td>
</tr>
<tr>
<td>V</td>
<td>0.96</td>
<td>0.95 – 0.98</td>
</tr>
</tbody>
</table>

3.2 Prevalence of patterns
In this population we found that the ulnar side of the hand was predominantly affected, with an affected ring finger in 386 hands (73%) followed by an affected little finger in 316 hands (60%) and middle finger in 130 hands (24%). With an affected thumb in 43 hands (8%) and an affected index finger in 36 hands (7%), the radial side of the hand was least often involved (Figure 8).

![Figure 8: Amount of affected fingers](image-url)
In Figure 9, end codes are shown in a binary fashion, with as 0 = not affected and 1 = affected, i.e. noduli, skin pits and contractures of all categories. By presenting the end codes in this way, 32 end codes \((2^5)\) were theoretically possible. Of these in our population 25 were actually present. In the complete group of patients the following five end codes were most prevalent: the end code 00010 – an affected ring finger only –, 00011 – a combination of an affected ring and little finger – 00001 – an isolated affected little finger –, 00111 – a combination of an affected middle, ring and little finger – and 00110 – a combination of an affected middle and ring finger. The remaining 20 end codes occurred in less than 5% of cases.

![Patterns of affected rays](image)

Figure 9: Patterns of affected hands with 25 different end codes. 0 = not affected, 1 = affected, i.e. noduli, skin pits and contractures of all categories.
When we looked specifically in the group of patients with an affected thumb (Figure 10), we identified the end code 10011 – the combination of an affected thumb with an affected ring and little finger – as the most frequently present end code (23%). Using Pearson’s $\chi^2$ test we found that in the group of patients with an affected thumb, the combination of an affected ring and little finger was significantly more often present than in the group of patients without radial involvement ($p = .033$).

![Figure 10: Prevalence of end codes in group of patients with an affected thumb.](image)

$0 =$ not affected, $1 =$ affected, i.e. noduli, skin pits and contractures of all categories.
We also noticed that in the group of patients with radial involvement the thumb was in isolated form affected in 9.3% and seen in associated form with one or more other affected rays in 90.7% (not shown). Furthermore, we found that an affected first ray was more frequently associated with a contracture of combined Iselin categories of the little finger, the ring finger and the combination of both ring finger and little finger than with contractures of other digits (Figure 11).

Figure 11: An affected thumb and associated contractures of combined Iselin categories of other rays.
3.3 Affected thumb and contractures of digit four and five
In total 531 hands were included, of which 255 left hands and 276 right hands. A list of patient characteristics and risk factors of Dupuytren disease (DD) is summarized in Table 7. Data was not complete for all characteristics. Data of 13 patients was missing for the variable epilepsy, data of 15 patients was missing for the variable diabetes mellitus and data of 17 patients for the variable liver disease. For excessive alcohol use and smoking, data of respectively 10 and 14 patients was missing. The variable family history was unknown in 9 patients and the characteristics duration of the disease and early onset of the disease were incomplete for respectively 30 and 24 patients. The percentage of missing data was equally divided over both groups.

Patients with an affected radial side of the hand were patients in which bilateral disease occurred significantly more often ($p = .028$) and consumed more alcohol ($p = .008$) compared to patients without involvement of the radial side of the hand.

Table 7: Characteristics and risk factors of patients with radial involvement and patients without radial involvement. Mean value is indicated when T-test was used, median value and inter quartile range is indicated when Mann Whitney U test was used and incidence when Pearson’s $\chi^2$ was used. *$p < .05$

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Radial side not affected (n= 461)</th>
<th>Radial side affected (n=70)</th>
<th>P value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65</td>
<td>66</td>
<td>.445b</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>340/121</td>
<td>57/13</td>
<td>.168</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>12 (2.6%)</td>
<td>1 (1.4%)</td>
<td>.580</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>41 (8.9%)</td>
<td>3 (4.3%)</td>
<td>.215</td>
</tr>
<tr>
<td>Liver disease</td>
<td>2 (0.4%)</td>
<td>0 (0%)</td>
<td>.587</td>
</tr>
<tr>
<td>Smoking</td>
<td>97 (21.0%)</td>
<td>20 (28.6%)</td>
<td>.104</td>
</tr>
<tr>
<td>Alcohol (&gt; 15 units / week)</td>
<td>63 (13.7%)</td>
<td>17 (24.3%)</td>
<td>.008*</td>
</tr>
<tr>
<td>Onset of disease &lt; 50 yr</td>
<td>133 (28.9%)</td>
<td>20 (28.6%)</td>
<td>.911</td>
</tr>
<tr>
<td>Positive family history</td>
<td>208 (45.1%)</td>
<td>25 (35.7%)</td>
<td>.161</td>
</tr>
<tr>
<td>Ectopic lesions</td>
<td>102 (22.1%)</td>
<td>13 (18.6%)</td>
<td>.344</td>
</tr>
<tr>
<td>Bilateral hand involvement</td>
<td>331 (71.8%)</td>
<td>59 (84.3%)</td>
<td>.028*</td>
</tr>
<tr>
<td>Duration of DD (years)</td>
<td>5 (7)</td>
<td>5 (13)</td>
<td>.750c</td>
</tr>
</tbody>
</table>

*Pearson’s $\chi^2$ test, bStudent T-Test, cMann Whitney U test.
Fisher’s exact test showed that radial side involvement was not associated with a mild contracture (Iselin stage II) of ring and little finger ($p = .728$) compared to patients without radial side involvement. On the contrary, we found a significant association ($p = .002$) between radial side involvement and a severe contracture (Iselin stage III and IV) of both ring and little finger compared to patients without involvement of the radial side of the hand (Table 8).

In this univariate analysis, incidence of bilateral hand involvement was 12.5% higher and the incidence of alcohol consumption of > 15 units per week was 10.6% higher in the group of patients with radial involvement. With a logistic regression analyses we investigated the influence of remaining variables and risk factors on radial side involvement. No variables influenced coefficient ‘$B$’ of radial involvement more than 10%, hence no variables were considered confounding factors. Therefore only radial involvement, alcohol consumption > 15 units/week and bilateral hand involvement were entered in the equation. After multivariate logistic regression analysis, none of the variables remained significant, but severe alcohol intake was very close to significance (Table 9).

### Table 8: Association between radial side involvement and severe contracture of ring and little finger. *$P < .05$*

<table>
<thead>
<tr>
<th>No radial involvement</th>
<th>Radial involvement</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No severe contracture digit IV and V</td>
<td>438</td>
<td>59</td>
<td>497</td>
</tr>
<tr>
<td>Severe contracture digit IV and V</td>
<td>23</td>
<td>11</td>
<td>34</td>
</tr>
<tr>
<td>Total</td>
<td>461</td>
<td>70</td>
<td>531</td>
</tr>
</tbody>
</table>

During logistic regression analyses, we noticed that alcohol consumption seemed to have a strong influence on the relation between radial involvement and a severe contracture of ring and little finger. This could indicate a mediator effect, whereby the effect of alcohol consumption on a severe contracture of ring and little finger could be explained by radial involvement. Extensive regression analyses (34) however showed no mediation.
4 Discussion

The aim of this study was to recognize patterns in the combination of affected rays and the severity of Dupuytren disease in relation to the affected rays and to known risk factors. We performed a large cross-sectional multi center study to identify these patterns.

For this study we included patients with primary Dupuytren disease, who were recruited between 2007 and 2011 from the outpatient clinics of the plastic surgery departments of six hospitals in the Netherlands in which both photographs of good quality and measured extension deficits were available. Of the 1201 hands that met our inclusion criteria, 531 hands could enter this study. Although we were able to perform a large multi center study and study more hands than most other studies did, we were disappointed about this drop in number and this may have caused bias. We lost most patients due to absence of photographs. Missing goniometry was mainly due to losing forms in the process. At this moment patient inclusion in the GODDAF study is being continued. To prevent such drop out in the future, more information for all concerned is necessary and more surveillance is needed in the different hospitals to make sure that patients are seen by the medical photographer and that forms with goniometry results are collected by designated persons and sent to the correct place.

Although Tubiana’s classification is most widely used for grading contractures, we chose to use Iselin’s classification in our study. This choice was mainly made because initial scoring method of this study was solely based on photographs. Iselin’s system has as shortcoming that it does not discriminate between an extension deficit of for instance the MCP joint of 5º and 90º. Both deficits are categorized as Iselin II. Therefore this scoring system is not suitable to study more nuances in severity of the disease.

In a pilot study, we assessed 56 hands according to the initial scoring method, thus exclusively assessment of photographs. During this pilot study, we became aware of the fact that possibly not all patients had held their hands in maximal extension, since fingers were in flexion without cords or skin changes showing. The agreement, measured with a weighted kappa, of this pilot appeared very low and ranged between 0.26 and 0.64. Therefore we concluded that assessment based solely on photographs was not reliable and we decided to combine photographs with actual measured contractures. After combining photographs with actual measurements the agreement was excellent and ranged from 0.84 to 0.96 between two different investigators (NK and RL) and from 0.92 to 0.96 between the first and second measurements of NK. Hereby we paid attention that actual measured extension deficit matched flexion contractures as seen in photographs. Yet, skin irregularities, nodes and cords without flexion contractures, were not documented and had to be assessed based on photographs. Since we wanted to study patterns in affected rays, this may have made our results less reliable, because invisible nodules may have been missed.

Main limitation of this study design is that we studied hands at one moment, while Dupuytren disease is a dynamical condition. It is not clear how patterns of the disease in our study population developed over time. Main limitation of our statistical analyses is that affected rays might be correlated. For this possible correlated data it might have been an option to use Generalized Estimating Equations (GEE) models.
Prevalence of patterns

We saw that the ring finger was affected in 386 hands (73%) followed by the little finger in 316 hands (60%) and the middle finger in 130 hands (24%). The radial side of the hand was less often affected, with the thumb in 43 hands (8%) and the index finger in 36 hands (7%). This order in affected rays supports the findings of Orlando in 1974, in which he studied 166 hands (31). He found that the ring finger was affected in 64% of the hands, the little finger in 55% of the hands, the middle finger in 45% and the thumb and index finger in respectively 8.4% and 7.4%. Luck (1959) however studied 206 hands and found a relatively high incidence of an affected thumb and first web space (35), just as Milner (2003), who studied 185 hands and found an affected ring finger in 59% of the hands, an affected little finger in 51% of the hands and an affected thumb and first web space in 28% of all hands, whereas the middle finger and index finger were affected in respectively 19% and 6% (33). Rayan declared in 2007 that the thumb and first web space were least often involved (36). Differences in these findings are probably due to differences in population characteristics and risk factors. But Dupuytren disease in the thumb received little attention over the years and since diagnosis in the thumb or first web space is not as easily made as in the other rays, it is also possible that an affected first ray was frequently missed.

The patterns that we found are broadly in line with the findings of Meyerding 1935 who studied 448 hands (21). However, he found more often the combination of an affected ring and little finger (45% versus 22% in our study) and less often an isolated affected ring finger (22% versus 27% in our study) or little finger (11% versus 19% in our study). These differences can be explained by the dynamical character of the disease. Other findings were consistent, although we identified more patterns than Meyerding described.

In the group of patients with radial involvement the thumb was in isolation affected in 9.3% and was associated with one or more other affected rays in 90.7%. We saw that in the latter group, the ring finger, little finger and the combination of ring finger and little finger were more frequently affected than other rays. This supports the findings of Tubiana who stated that an affected radial side is almost always accompanied by an affected ulnar side (23). We also saw that the combination of an affected ring and little finger occurred significantly more often in the group of patients with radial involvement than in patients without an affected thumb. Furthermore, we found that an affected first ray was most frequently associated with a contracture of the little finger (26%), the ring finger (16%) and the combination of both ring finger and little finger in 12% of the hands, suggesting an association between the thumb and the ulnar side of the hand.

In the univariate analyses we saw that an affected radial side was significantly associated with a contracture of the ring and little finger. When we differentiated between the severity of the contractures of digits IV and V, we saw that an affected radial side was not associated with a mild contracture of ring and little finger, but only a severe contracture of the ring and little finger showed a highly significant (P = .002) association with the radial side. These results suggest that there seems to be an association between the thumb and a more severe type of Dupuytren disease. However, after multivariate logistic regression analysis, adjusted for the variables bilateral hand involvement and alcohol consumption > 15 units / week, radial involvement was not significant anymore.
Patient characteristics and risk factors
Patients with radial involvement were on average one year older than patients without radial involvement and did not have a significant difference in duration of the disease. These findings suggest that Dupuytren disease in the radial side of the hand does not occur in a younger group of patients and that patients with their radial side affected do not have a tendency toward rapid progression. These results support the study of Milner in 2003 who found that patients with an affected thumb were on average eight years older and suffered on average five years longer from Dupuytren disease, suggesting that an affected radial side was not related to diathesis features (33).

Alcohol
A remarkable finding in this study was that alcohol consumption seemed to have a strong influence on the association between radial involvement and a severe contracture of ring and little finger. We considered the possibility of a mediator effect, whereby radial involvement could explain the effect of alcohol consumption on a severe contracture of ring and little finger. Thus, the hypothesis was that alcohol consumption could cause radial involvement, which in turn led to a severe contracture of ring and little finger. We tested this by performing several logistic regression analyses, whereby we studied the influence of the three variables on each other. Nevertheless, mediation could not be confirmed.

The relation between alcohol and Dupuytren disease remains unclear. A long time it was thought that patients with Dupuytren disease were alcoholics based on one case report. In 1987 a prospective study was performed to study especially the relationship between Dupuytren disease, alcohol consumption and liver disease (37). They concluded that alcohol rather than chronic liver disease was an etiologic factor in Dupuytren disease. Other studies showed an association between alcohol induced liver disease and Dupuytren disease (38,39). Yet, the mechanism and degree of contribution remains unclear.

5. Conclusion
Our study is the first to show 25 patterns in Dupuytren affected rays. The following three patterns were most frequently present: a combination of an affected ring and little finger, a combination of an affected middle, ring and little finger and a combination of an affected middle and ring finger. Additionally we found a pattern of an affected thumb and an affected ring and little finger.

Our study gives an overview of patterns in Dupuytren disease, and shows in particular a possible influence of alcohol on a severe contracture of ring and little finger, especially in patients with an affected thumb.
6. Acknowledgements
Hereby I would like to thank Prof. dr. P.M.N. Werker, for his supervision and support during this process and for critically reviewing the manuscript, and Rosanne Lanting for her enthusiasm and her supervision and willingness to help whenever possible to improve this study. I enjoyed working together.

I also thank Guido Dolmans for providing access to the GODDAF database; Bert Tebbes for providing the photographs of Dupuytren disease; Xavier Keuter, Marius Kemler, Anneke Knepper, Guus Vermeulen and Oliver Zöphel for coordinating the study in different hospitals in the Netherlands; Sterre Payens and Freek Corsten for their administrative work; Shariselle Pool and Anna Randag for discovering SPSS together; Judith Vonk for her help with statistical analysis and all the patients with Dupuytren disease for participating in this study.
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8. Appendices

Appendix 1: Vragenlijst arts
# Genetisch onderzoek Dupuytren

Ruimte voor ponsplaatje, of zelf invullen

## Vragenlijst arts

<table>
<thead>
<tr>
<th>Naam:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Voorletters:</td>
<td></td>
</tr>
<tr>
<td>Geb. datum:</td>
<td></td>
</tr>
<tr>
<td>Geslacht:</td>
<td></td>
</tr>
</tbody>
</table>

### Algemeen

1. Wat is de datum van vandaag? [ ]

2. Welke hand(en) zijn aangedaan met de ziekte van Dupuytren?
   - [ ] linkerhand  
   - [ ] rechterhand  
   recidief: [ ] ja  [ ] nee  

### Extensiebeperking

<table>
<thead>
<tr>
<th></th>
<th>Dig 1 (L/R)</th>
<th>Dig II (L/R)</th>
<th>Dig III (L/R)</th>
<th>Dig IV (L/R)</th>
<th>Dig V (L/R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3. Extensie beperking voor MCP</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
</tr>
<tr>
<td>4. Extensie beperking voor P(IP)</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
</tr>
<tr>
<td>5. Extensie beperking voor DIP</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
<td>.....°/ .....°</td>
</tr>
</tbody>
</table>

### Ectopische locaties:

<table>
<thead>
<tr>
<th></th>
<th>Dig 1 (L/R)</th>
<th>Dig II (L/R)</th>
<th>Dig III (L/R)</th>
<th>Dig IV (L/R)</th>
<th>Dig V (L/R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Knucklepads</td>
<td>[ ] ja  [ ] nee</td>
<td>[ ] ja  [ ] nee</td>
<td>[ ] ja  [ ] nee</td>
<td>[ ] ja  [ ] nee</td>
<td>[ ] ja  [ ] nee</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>(L/R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. M. Ledderhose:</td>
<td>[ ] ja  [ ] nee  [ ] beginnend</td>
</tr>
<tr>
<td>8. M. Peyronie:</td>
<td>[ ] ja  [ ] nee  [ ] niet gecontroleerd</td>
</tr>
</tbody>
</table>
Appendix 2: Vragenlijst patiënt
**Phenotype of Dupuytren’s disease**

**N.S.S. Kornmann**

**Vragenlijst genetisch onderzoek**

**Ziekte van Dupuytren**

IN TE VULLEN DOOR DE PATIËNT

---

### Algemeen

<table>
<thead>
<tr>
<th>Wat is de datum van vandaag?</th>
<th>………-……. 20…….(dd-mm-20jj)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wat is uw geboortedatum?</td>
<td>………-……. 19…….(dd-mm-19jj)</td>
</tr>
</tbody>
</table>
| Wat is uw geslacht?         | □ man  
□ vrouw |
| Hoeveel scholing heeft u gehad? | □ lagere school niet afgemaakt  
□ lagere school  
□ middelbare school niet afgemaakt  
□ middelbare school  
□ lbo  
□ mbo  
□ hbo  
□ universiteit |
| Wat is uw etnische afkomst?  | □ Nederlands, welke stad/dorp…………………………………… |
| Ofwel waar komen u en uw familie oorspronkelijk vandaan? | □ Ander Europees land, namelijk…………………………………… |
| Dit is belangrijk voor het erfelijkheidsonderzoek. | □ Marokkaans  
□ Surinaams / Antilliaans  
□ Turks  
□ Aziaatisch  
□ Anders, namelijk…………………………………… |
| Welke omschrijving geeft uw situatie het beste weer? | □ momenteel werkzaam  
als:…………………………………… |
| □ ziekewet  
□ werkeloos  
□ VUT/ AOW/pensioen  
□ student / scholier  
□ Anders,  |
| namelijk…………………………………… |

De ziekte van Dupuytren komt meer voor bij mensen die veel met de handen hebben gewerkt. Heeft u veel werk met de handen gedaan? Zo ja, wat voor werk

□ nee (bv kantoorbaan)  
□ ja,  
nl………………………………………………………………………………………………………………
Hoe lang heeft u zwaar werk gedaan?
- nooit
- 1-5 jaar
- 6-10 jaar
- 11-15 jaar
- 16-20 jaar
- 21-25 jaar
- 26-30 jaar
- meer dan 30 jaar

Heeft u hobby’s of doet u aan sporten die handarbeid vragen?
- nee
- ja,
  nl……………………………………………………………..
  ………………………………………………………………….

Maakt u gebruik van of bent u van plan gebruik te maken van een of meer van de volgende regelingen?

<table>
<thead>
<tr>
<th>Gebruik van</th>
<th>Aangevraagd</th>
<th>Van plan te gebruiken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ja</td>
<td>Nee</td>
<td>Ja</td>
</tr>
<tr>
<td>Ziektewet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WIA (vroeger WAO)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WW</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ziekte van Dupuytren

Bent u links of rechtshandig?
- linkshandig
- rechtshandig
- dubbelhandig

Komt de ziekte van Dupuytren in uw familie voor?
- ja, bij (omcirkel bij wie): Grootvader, grootmoeder, vader, moeder, broer(s), zuster(s), oom, tante, neef/neven, nicht(en), zoon(s), dochter(s)
- nee
- weet niet

Hoe lang heeft u afwijkingen in uw hand(en) die passen bij de ziekte van Dupuytren?
- 1 jaar
- 2 jaar
- 3 jaar
- 4 jaar
- 5 jaar
- 6 jaar
- 7 jaar
- 8 jaar
- 9 jaar
- 10-19 jaar
- meer dan 20 jaar
- weet niet

In welke leeftijdsgroep bevond u zich toen u voor het eerst harde knobbels in de handpalmen of kromme vingers opmerkte?
- 0-9 jaar
- 10-19 jaar
- 20-29 jaar
- 10-19 jaar
- 20-29 jaar
- 30-39 jaar
- 40-49 jaar
- 50-59 jaar
- 60-69 jaar
- 70-79 jaar
- meer dan 90 jaar
- meer dan 20 jaar
- 80-89 jaar
- weet niet

Zoals u wellicht weet kan de ziekte van Dupuytren ook op andere plaatsen in het lichaam voorkomen. De vingerknokkels
Phenotype of Dupuytren's disease

35

N.S.S. Kornmann

(knucklepads), voetzool (ziekte van Ledderhose) en penis (ziekte van Peyronie).

<table>
<thead>
<tr>
<th>Knucklepads zijn knobbels op het gewricht tussen het eerste en tweede vingerkootje. Heeft u knucklepads?</th>
<th>□ ja</th>
<th>□ ik denk het wel</th>
<th>□ nee</th>
<th>□ weet niet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heeft u ook verhardingen of knobbels onder de voetzool??</td>
<td>□ ja</td>
<td>□ ik denk het wel</td>
<td>□ nee</td>
<td>□ weet niet</td>
</tr>
</tbody>
</table>

De volgende vraag is alleen voor mannen. Bij de ziekte van Peyronie ontstaan er verhardingen in de penisschacht. Deze verhardingen kunnen tijdens de erectie een kromstand veroorzaken.

| Heeft u de ziekte van Peyronie? | □ ja | □ ik denk het wel | □ nee | □ weet niet |

Klachten en behandeling van de ziekte van Dupuytren

| Welke klachten heeft u van de ziekte van Dupuytren (meerdere antwoorden mogelijk)? | □ geen klachten | □ moeite met handen in zakken stoppen | □ moeite met handschoenen aantrekken | □ moeite met dagelijkse bezigheden | □ de hand blijft soms haken | □ moeite met handen geven | □ problemen bij werk | □ pijn | □ moeite hobby’s, namelijk…………………………………………………………………… | □ anders, nl…………………………………………………………………… |
**Waarom wilt u geopereerd worden (meerdere antwoorden mogelijk)?**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>○</td>
<td>omdat ik er last van heb</td>
</tr>
<tr>
<td>○</td>
<td>omdat ik bang ben dat de vingers steeds krommer gaan staan</td>
</tr>
<tr>
<td>○</td>
<td>advies van de huisarts</td>
</tr>
<tr>
<td>○</td>
<td>advies van de plastisch chirurg</td>
</tr>
<tr>
<td>○</td>
<td>anders, nl……………………………………………………………</td>
</tr>
</tbody>
</table>

**Is uw hand ooit eerder geopereerd wegens de ziekte van Dupuytren? Zo ja in welk jaar?**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>○</td>
<td>nee</td>
</tr>
<tr>
<td>○</td>
<td>ja, linkerhand in (jaartal) …………………………………</td>
</tr>
<tr>
<td>○</td>
<td>ja, rechterhand in (jaartal) ………………………………</td>
</tr>
</tbody>
</table>

**Is uw hand ooit eerder geopereerd vanwege iets anders dan de ziekte van Dupuytren? Zo ja in welk jaar en waarom?**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>○</td>
<td>nee</td>
</tr>
<tr>
<td>○</td>
<td>ja, linkerhand in (jaartal) …………………………………</td>
</tr>
<tr>
<td></td>
<td>ivm……………………………………………………………</td>
</tr>
<tr>
<td></td>
<td>………………………………………………………………..</td>
</tr>
<tr>
<td>○</td>
<td>ja, rechterhand in (jaartal) ………………………………</td>
</tr>
<tr>
<td></td>
<td>ivm……………………………………………………………</td>
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</tbody>
</table>

**Wat ziet u zelf als een mogelijke oorzaak van de ziekte van Dupuytren bij uzelf?**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>○</td>
<td>geen idee</td>
</tr>
<tr>
<td>○</td>
<td>veel zware handarbeid gedaan</td>
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<tr>
<td>○</td>
<td>komt in de familie voor</td>
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<tr>
<td>○</td>
<td>handletsel, nl……………………………………………………………</td>
</tr>
<tr>
<td>○</td>
<td>anders, nl……………………………………………………………</td>
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</tbody>
</table>

**Heeft u een van de nevenstaande ziekten doorgemaakt (meerdere antwoorden mogelijk)?**

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>○</td>
<td>epilepsie</td>
</tr>
<tr>
<td>○</td>
<td>suikerziekte</td>
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<tr>
<td>○</td>
<td>leverziekte door alcohol gebruik</td>
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</tbody>
</table>

**Gebruikt u pijnstillers?**

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<table>
<thead>
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<tbody>
<tr>
<td>○</td>
<td>nee</td>
</tr>
<tr>
<td>○</td>
<td>ja, paracetamol</td>
</tr>
<tr>
<td>○</td>
<td>ja, aspirine, ascal</td>
</tr>
<tr>
<td>○</td>
<td>ja, ibuprofen, brufen, nerofen, advil, diclofenac, arthrotec, voltaren, naproxen, naprosyne</td>
</tr>
<tr>
<td>○</td>
<td>anders, nl……………………………………………………………</td>
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</tbody>
</table>

**Gebruikt u bloedverdunners?**

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<table>
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<tbody>
<tr>
<td>○</td>
<td>nee</td>
</tr>
<tr>
<td>○</td>
<td>ja, aspirine, ascal, acetosal, kinderaaspirine, ascal cardio</td>
</tr>
<tr>
<td>○</td>
<td>ja, sintrom, sintromitis, marcoumar</td>
</tr>
<tr>
<td>○</td>
<td>anders, nl……………………………………………………………</td>
</tr>
</tbody>
</table>
### Phenotype of Dupuytren's disease

**N.S.S. Kornmann**

#### Gebruikt u medicijnen tegen suikerziekte?
- □ nee
- □ ja, insuline
- □ anders, nl…………………………………………………………………………………………

#### Gebruikt u middelen tegen epilepsie?
- □ nee
- □ ja, tegretol, carbamazepine
- □ ja, depakine
- □ ja, fenobarbital
- □ ja, eytoine
- □ ja, rivotril
- □ anders, nl………………………………………………………………………………………..

#### Gebruikt u andere medicijnen?
- □ nee
- □ ja, nl…………………………………………………………………………………………

#### Overige vragen

##### Hoeveel alcoholische consumpties (eenheden) drinkt u per week (als 1 consumptie telt bijvoorbeeld 1 glas bier, 1 glas wijn, 1 glas jenever)?
- □ geen
- □ 1-2 per week
- □ 3-5 per week
- □ 6-10 per week
- □ meer dan 20 per week

##### Rookt u?
- □ ja
- □ nee
- □ niet meer sinds …………

##### Indien u rookt: hoeveel per dag?
- □ 1-2 per dag
- □ 3-5 per dag
- □ meer dan 20 per dag
- □ 6-10 per dag

##### Bent u allergisch?
- □ ja
- □ nee
- □ weet niet

Dank voor het invullen!