

Foot & Ankle International

<http://fai.sagepub.com/>

Association of Morbus Ledderhose With Dupuytren's Contracture

Kristján G. Gudmundsson, Thorbjörn Jónsson and Reynir Arngrímsson

Foot Ankle Int published online 5 February 2013

DOI: 10.1177/1071100713475352

The online version of this article can be found at:

<http://fai.sagepub.com/content/early/2013/02/04/1071100713475352>

Published by:



<http://www.sagepublications.com>

On behalf of:



[American Orthopaedic Foot & Ankle Society](#)

Additional services and information for *Foot & Ankle International* can be found at:

Email Alerts: <http://fai.sagepub.com/cgi/alerts>

Subscriptions: <http://fai.sagepub.com/subscriptions>

Reprints: <http://www.sagepub.com/journalsReprints.nav>

Permissions: <http://www.sagepub.com/journalsPermissions.nav>

>> [OnlineFirst Version of Record](#) - Feb 5, 2013

[What is This?](#)

Association of Morbus Ledderhose With Dupuytren's Contracture

Foot & Ankle International
XX(X) 1–5
© The Author(s) 2013
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/1071100713475352
http://fai.sagepub.com

Kristján G. Gudmundsson, MD, PhD^{1,2}, Thorbjörn Jónsson, MD, PhD^{2,3},
and Reynir Arngrímsson, MD, PhD^{4,5}

Abstract

Background: Fibromatous nodules in the sole of the foot are often called Ledderhose disease. It is a benign nodular formation in the plantar aponeurosis, typically at the distal medial border. A lump forms and it can be a few centimeters in diameter. It is frequently seen as an isolated disease, but a relationship to Dupuytren's has been noted in some patients.

Methods: The study was a part of a large cohort study, the Reykjavík study. Men with Dupuytren's disease (n = 122) were invited to follow-up 18 years after the initial observation. An equal number of controls, matched for age and smoking habits, were also invited. A total of 92 Dupuytren's patients and 101 control subjects attended for follow-up and were examined for plantar nodules. Statistical evaluation was carried out using chi-square test and presented as odds ratio (OR) and 95% confidence interval (95% CI).

Results: Ledderhose disease was identified in 14 of the 92 (15.2%) men with Dupuytren's disease, while it was only in 4 of the 101 (3.9%) matched controls (OR = 4.35, 95% CI, 1.3–16.7, $P < 0.01$). Men operated for Dupuytren's disease or with finger contractures were more likely to have plantar nodules than those with only nodules or strings in the palms (OR = 6.1, 95% CI, 1.8–27.1, $P < 0.001$). The plantar involvement was related to family history of Dupuytren's disease (OR = 3.1, 95% CI, 1.1–8.5, $P = 0.02$).

Conclusion: Men with manifestations of finger contractures or who need surgery for Dupuytren's disease are more likely to also develop plantar fibromas.

Level of Evidence: Level III, retrospective comparative series.

Keywords: Ledderhose disease, Dupuytren's disease, epidemiology, plantar fibromatosis, plantar fascia

In 1897 Professor Ledderhose described 50 cases of a disease that affected the plantar fascia with fibromatosis and this condition has since been associated with his name.¹⁹ Baron Dupuytren had observed nodules in the feet of his patients with finger contractures.⁹ Fibromatosis is nevertheless often solely observed in the aponeurosis of the feet and it has been suggested to be an independent disorder.¹⁴ Dupuytren's disease is common in Caucasians in Northwestern Europe with yearly incidence of 2.9% and prevalence up to 40% in 70-year-old Icelandic males.^{12,13} In other parts of the world the disease is regarded as much less common.^{7,13}

The actual prevalence of plantar fibromatosis in the general population is unknown. However, the prevalence has been documented in several cohort studies of Dupuytren's disease.^{1,3,4,8,11,17,22} The disease has been described in children from early childhood and adults reaching old age. Its incidence is most common between the ages of 50 to 60 years, with striking male predominance.¹⁴ Ledderhose disease has been reported to have a strong familial predisposition.⁵ It has also been related to other forms of extra palmar involvement, including the knuckle pads and Peyronies disease.^{4,17}

Plantar fibromatosis is most often situated along the medial border of the foot, in the nonweightbearing part of

the plantar aponeurosis. The disease begins as a small nodule, which is sometimes painful. It grows in a time span of years, often forming a mass of several centimeters in diameter. Sometimes the mass grows to the extent of causing discomfort while walking and even flexion deformities of the toes.^{6,10} Interestingly, the histopathology is the same as seen in the palmar fascia in Dupuytren's disease.²⁵ The nodules are always benign.¹⁴ The differential diagnoses are other space-occupying tumors such as osteosarcoma.² A conservative approach is recommended if the lesion is not causing discomfort.²⁵ The treatment has been surgical removal of the involved fascia.^{6,14,23} The overall recurrence rate is up to 60%.²⁴ Radiation therapy has been used as an

¹Reykjavík Primary Health Care, Glaesibaer, Reykjavík, Iceland

²University of Iceland, Reykjavík, Iceland

³The Blood Bank, Landspítali University Hospital, Reykjavík, Iceland

⁴Department of Genetics and Molecular Medicine, Landspítali University Hospital

⁵Department of Biochemistry and Molecular Biology, BioMedical Center, University of Iceland, 101 Reykjavík, Iceland

Corresponding Author:

Kristján G. Gudmundsson, MD, PhD, Reykjavík Primary Health Care, Glaesibaer, Alfreimur 74, 104 Reykjavík, Iceland
Email: kristgud@simnet.is

alternative treatment, with complete or partial remission in 88% of cases at 22 months follow-up.¹⁵ Here we present the results from a large population-based cohort study, describing Ledderhose plantar nodules and their relationship with Dupuytren's disease, age, and family history.

Methods

Study Subjects

As a part of a large national epidemiological cohort study, the Reykjavik study, 1297 men were evaluated for signs of Dupuytren's disease in 1981 to 1982 and 249 (19.2%) at that time had signs of Dupuytren's disease.^{12,13} On reevaluation in 1999, 122 (49.0%) were still alive and all were invited for a follow-up. As a control group equal numbers of men that had participated in the Reykjavik study at the same time and were symptom free in 1981 to 1982 were also invited. The control group was matched for age and smoking habits. All participants in the case control study in 1999 were invited with a letter and those that did not respond were contacted by telephone. At the Heart Preventive Clinic the participants answered a questionnaire created for this study that included questions about the symptoms of Dupuytren's and Ledderhose diseases, demographic and social factors, occupation, and other health-related conditions. They were also questioned about the occurrence of contracted fingers in other family members. Participants were asked to recall when they first noticed disease in the palm. The study was free of charge. The study was approved by the National Bioethics Committee (licence number 08-131) and the Data Protection Authority in Iceland. The study was carried out in accordance with the World Medical Association declaration of Helsinki and all subjects signed informed consent.

Classification of the Disease

The hands and feet were examined by the same physician and classified as: (a) normal; (b) palpable palmar nodules larger than 5 mm, skin tethering, and/or fibrous cord(s); (c) contracted fingers; and (d) operated due to contractures. The feet were examined and soles palpated and the presence or absence of nodules registered. The classification system has been used in other epidemiological studies.^{7,16} To diminish the potential for observer bias, the study was planned with the observer not having information about the original group allocation of the participants at the time of examination. Single observer approach was used to reduce interobserver variation in the study.

Statistical Evaluation

The present investigation was a nested case control study, derived from a large-scale epidemiological study in

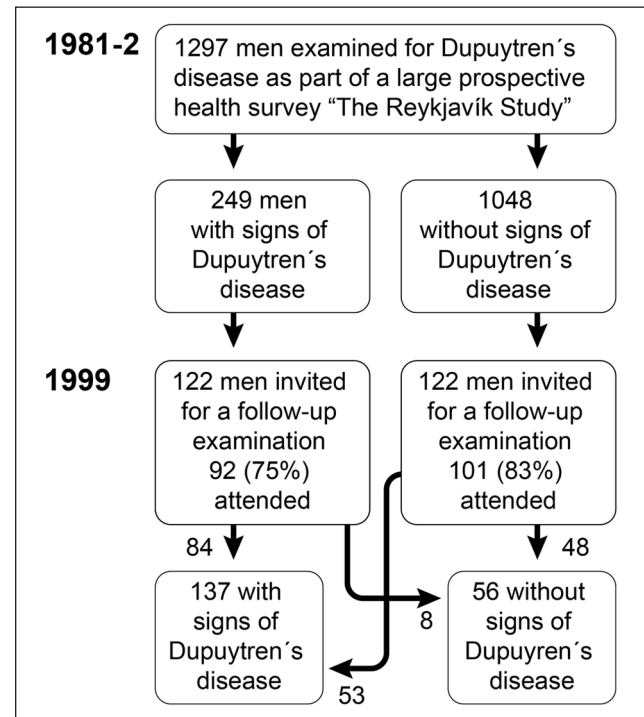


Figure 1. Design of the study. The clinical examiners were blinded to the original disease status and classification. As Dupuytren's contracture is a disease with a high incidence in elderly males, 56 of the 101 controls had developed signs of Dupuytren's disease in the hand when reexamined. In 8 subjects palmar involvement was not confirmed. The final study groups included 137 subjects defined as cases with Dupuytren's disease and 56 Dupuytren's-free control subjects.

Reykjavik, Iceland.^{12,13} Primary outcome was defined as the difference in Ledderhose prevalence between the cases and controls in the original study groups, namely, patients with Dupuytren's disease and matched control in 1981 to 1982. As Dupuytren disease has been shown to have age-dependent prevalence,^{12,13} secondary outcomes were the difference in Ledderhose prevalence in subjects with Dupuytren's contractures in 1999 compared to those that did not, association with family history, and age of onset of Dupuytren's disease. Of the 122 men with Dupuytren's disease in the 1981 to 1982 cohort, 92 (75%) attended the clinic for follow-up. Eight of these men did not have signs of the disease at the time of follow-up (Figure 1). Of the original 122 controls, a total of 101 (83%) attended. As Dupuytren's disease is common with high annual incidence in elderly men in Iceland,^{12,13} part of this initial control group from 1981 to 1982 had at the reevaluation in 1999 developed palmar disease ($n = 53$). These were also considered as cases in the secondary outcome evaluation, and in this respect the final study group comprised of 137 cases with Dupuytren's disease and 56 control subjects.¹²

Table 1. Association Between Ledderhose and Dupuytren's Disease: Number of Subjects With Ledderhose Disease Classified According to the Presence of Dupuytren's Disease in 1999.

Dupuytren's Status	Ledderhose Disease	
No sign of Dupuytren's disease (n = 56)	0	0%
Nodule in the palm greater than 5 mm (n = 26)	1	3.8%
Induration, cord in palm (n = 54)	3	5.6%
Contracted finger (n = 29)	4	13.8%
Operated on (n = 28)	10	35.7%
Total with Dupuytren's (n = 137)	18	13.1%

Table 2. Relation Between Family History of Dupuytren's Disease and the Presence of Nodules in the Plantar Fascia (Ledderhose Disease)

Family History of Dupuytren's Disease	With Ledderhose Disease	
No (n = 99)	9	9.1%
Yes (n = 38)	9	23.7%

Four men had family history of Dupuytren's disease without being affected of the disease.

Statistical significance was evaluated with the chi-square test and Yates correction when appropriate. Results are presented as odds ratio (OR) and 95% confidence interval (CI). The significance level was set at $P < 0.05$.

Results

When comparing the prevalence of Ledderhose disease in the nested-case control study in 1981 to 1982, 14 of the 92 (15.2%) men with Dupuytren's disease had the condition while it was only observed in 4 of the 101 (3.9%) matched controls (OR = 4.35, 95% CI, 1.3-16.7, $P < 0.01$). For secondary outcome evaluation of the 1999 data, all patients with Dupuytren's contractures were compared to those that did not have the condition. Of those with signs of Dupuytren's disease (n = 137), 18 or 13.1% had plantar involvement. None of the 56 men in the disease-free group were found to have plantar disease (Table 1). Men who had been operated on or had contracted fingers were more likely to have plantar nodules than those with a string or a nodule (>5 mm) in the palm (OR = 6.1, 95% CI, 1.8-27.1, $P < 0.001$). Investigation of the possible association between Ledderhose disease and family history of Dupuytren's disease showed that 9 out of the 38 participants with Dupuytren's diseases and positive family history had plantar involvement (Table 2). Of those 99 participants with Dupuytren's disease without family history, 9 had signs of Ledderhose disease (OR = 3.1, 95% CI, 1.1-8.5, $P = 0.02$). Most of the men with Dupuytren's disease could not recall the age when their

hands became affected, but of the 18 men found to have Ledderhose disease, 13 did. When comparing those who had the first signs of Dupuytren's disease before the age of 50 years (n = 9 out of 28) to those developing signs at a later age (n = 4 out of 30), a trend toward association between early age at onset and predisposition of plantar affection was observed (OR = 3.0, 95% CI, 0.7-15.5; $P < 0.096$).

Discussion

In Ledderhose disease, fibrous nodules form in the plantar fascia of the feet, which sometimes can disturb walking and be painful.^{15,21} The Dupuytren's diathesis is a complicated condition where the etiology is still a mystery.²⁰ Both conditions reduce quality of life and cause functional disability in a surprisingly large proportion of the general population in Northwestern Europe.^{7,13,15,21} The most interesting observation in this study was that all of the men with signs of Ledderhose disease also had Dupuytren's disease. This supports the notion that Dupuytren's and Ledderhose disease have a common etiology and underlying pathology. In the clinical setting, such information could be diagnostically helpful in patients with mass in the aponeurosis of the foot.

The approach applied in this study, where the data were derived from an unselected population-based cohort study, is a considerable strength. All studies of retrospective nature may be subjected to biases. Possible biases in this study may be related to the idea that a palpable nodule of 5 mm under the skin in the fascia of the foot and hand may be difficult to detect with accuracy and can be considered a subjective finding by the observer. Hence an underestimate of the true prevalence would be expected. The observer did not have access to the original group allocation and thus did not know if he was questioning and examining a participant from the original Dupuytren's or control group. This blinding was done to reduce the risk of observation bias. By applying single examiner approach, interobserver bias was also minimized. Interestingly, a 2.9% annual incidence of Dupuytren's disease in this cohort over the 18-year follow-up period was observed.^{12,13} We could not confirm the diagnosis in 8 cases of the original cohort. None of these had signs of Ledderhose disease. The most likely explanation is that this is an effect of spontaneous regression of the palmar nodules, which is a well-described phenomenon in patients with early stages of Dupuytren's disease.¹⁸ For this reason the data were stratified for secondary outcome evaluation with all those with Dupuytren's disease compared to those disease free in 1999. Under both approaches, namely, examining the data by using the original classification from 1981 to 1982 cohort or the secondary evaluation of the data using the 1999 stratification, there was significant association between Dupuytren's disease and Ledderhose plantar nodules. Recall bias may also limit conclusions that can be drawn from a retrospective study, for example, low proportion could accurately

Table 3. Prevalence of Ledderhose Disease in This Study Compared to Previously Published Studies

Author	Year	Total (n)	Ledderhose(n)	(%)	Reference
Allen et al	1955			9.0%	1
Gordon	1964	101	9	8.9%	11
Hueston	1972	159	19	12.0%	16
Caroli et al	1991	352		6.0%	4
Brenner et al	2001	566	21	3.7%	3
Degreeef and Smet	2008	65	12	19.0%	7 ^a
Gudmundsson et al	2012	137	18	13.2%	Present study ^b

^aWomen only.^bMen only.

remember when the condition started and when they first noticed symptoms of the disease. Half of the subjects with Ledderhose disease claimed they had a family history of Dupuytren's disease. Here underreporting rather than an overestimate would be expected. Present results can be compared to previous findings where the prevalence of Ledderhose disease is around 2% to 18% in those with Dupuytren's disease (Table 3). However, the prevalence of Ledderhose disease in an unselected population has not previously been described. Pickren and coworkers observed in 1951 that 3.3% of 120 cases of plantar fibromatosis had a family history of Dupuytren's disease compared to 50% in our sample. In their sample 53% had coexistent palmar involvement.²¹ Caroli and coworkers pointed out that the simultaneous presence of knuckle pads and Dupuytren's and Ledderhose disease was statistically related to each other. He proposed that the presence of these fibromatous conditions was a presentation of the same phenotype.⁴

In summary, men with the manifestations of finger contractures or in the need for surgery for Dupuytren's disease were more likely to develop plantar fibromas. Ledderhose disease was more common among Dupuytren's patients when a family history of Dupuytren's was present.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) declared receipt of the following financial support for the research, authorship, and/or publication of this article: The study was supported by research grants from the Icelandic Centre for Research and the Science Fund of Family Physicians in Iceland.

References

- Allen RA, Woolner LB, Ghormley RM. Soft tissue tumors of the sole. *J Bone Joint Surg Am.* 1955;37A:14-26.
- Aviles E, Arlen M, Miller T. Plantar fibromatosis. *Surgery.* 1971;69:117-120.
- Brenner P, Krause-Bergmann A, Van VH. Dupuytren contracture in North Germany. Epidemiological study of 500 cases. *Unfallchirurg.* 2001;104:303-311.
- Caroli A, Zanasi S, Marcuzzi A, Guerra D, Cristiani G, Ronchetti PI. Epidemiological and structural findings supporting the fibromatous origin of dorsal knuckle pads. *J Hand Surg (Br).* 1991;16B:258-262.
- Chen KT, Van Dyne TA. Familial plantar fibromatosis. *J Surg Oncol.* 1985;29:240-241.
- Classen DA, Hurst LN. Plantar fibromatosis in bilateral flexion contractures: a review of the literature. *Ann Plast Surg.* 1992;28:475-478.
- Degreeef I, De Smet L. A high prevalence of Dupuytren's disease in Flanders. *Acta Orthop Belg.* 2010;76:316-320.
- Degreeef I, Steeno P, De Smet L. A survey of clinical manifestations and risk factors in women with Dupuytren's disease. *Acta Orthop Belg.* 2008;74:456-460.
- Dupuytren G. *Lecons orales de Clinique chirurgicale faites a l'Hotel Dieu de Paris.* Paris: Germer Bailliere; 1839.
- Farsetti P, Tudisco C, Caterini R, Bellocci M. Ledderhose's disease: case study with histologic and ultrastructural analysis. *Ital J Orthop Traumatol.* 1992;18:129-133.
- Gordon SD. Dupuytren's contracture: plantar involvement. *Br J Plast Surg.* 1964;17:412-413.
- Gudmundsson KG, Arngrimsson R, Jonsson T. Eighteen years followup study of the clinical manifestations and progression of Dupuytren's disease. *Scand J Rheumatol.* 2001;30:31-34.
- Gudmundsson K, Arngrimsson R, Sigfusson N, Bjornsson A, Jonsson T. Epidemiology of Dupuytren's disease: clinical, serological, and social assessment. The Reykjavik Study. *J Clin Epidemiol.* 2000;53:291-296.
- Haedicke JG, Sturim S. Plantar fibromatosis. An isolated disease. *Plast Reconstr Surg.* 1989;83:296-300.
- Heyd R, Dorn AP, Herkstroter M, Rodel C, Muller-Schimpfle M, Fraunholz I. Radiation therapy for early stages of morbus Ledderhose. *Strahlenther Onkol.* 2010;186:24-29.
- Hueston JT. The incidence of Dupuytren's contracture. *Med J Aust.* 1960;6:999-1002.

17. Hueston JT. The management of ectopic lesion in Dupuytren's disease. In: Hueston JT, Tubiani R, eds. *Dupuytren's Disease*. 2nd ed. Edinburg: Livingston; 1978.
18. Hueston JT. Regression of Dupuytren's contracture. *J Hand Surg Br*. 1992;17(4):453-457.
19. Ledderhose G. Zur Pathologi der Aponeurose des Fusses und der Hand. *Arch Klin Chir*. 1897;55:694.
20. Picardo NE, Khan WS. Advances in the understanding of the aetiology of Dupuytren's disease. *Surgeon*. 2012;10:151-158.
21. Pickren JW, Smith AG, Stevenson TW, Staut AP. Fibromatosis of the plantar fascia. *Cancer*. 1951;4:846-856.
22. Sammarco GJ, Mangone PG. Classification and treatment of plantar fibromatosis. *Foot Ankle Int*. 2000;21:563-569.
23. Skoog T. Dupuytren's contracture with special reference to etiology and improved surgical treatment: its occurrence in epileptics, note on Knuckle pads. *Acta Chir Scand*. 1948;Suppl 139:1-190.
24. van der Veer WM, Hamburg SM, de Gast A, Niessen FB. Recurrence of plantar fibromatosis after plantar fasciectomy: single-center long-term results. *Plast Reconstr Surg*. 2008;122:486-491.
25. White SW. Plantar fibromatosis. *Arch Dermatol*. 1981;117:375-376.