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Prevalence of Peyronie and Ledderhose Diseases in a Series of 730 Patients with Dupuytren Disease

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Background: Dupuytren, Peyronie, and Ledderhose diseases are related fibroproliferative disorders characterized by abnormalities in the connective tissue of the palm of the hand, the tunica albuginea of the penis, and the sole of the foot, respectively. Concomitant prevalence rates of these diseases have only been described in a few small populations. This article aims to report on a large population and to raise awareness in surgeons treating Dupuytren disease for concurring related fibroproliferative disorders.

Methods: Patients diagnosed as having Dupuytren disease were recruited from outpatient clinics in the northern part of the Netherlands from 2007 to 2016. Questionnaires concerning demographics, clinical characteristics, the coexistence of Ledderhose and/or Peyronie diseases, and other factors were filled in by the participants and by plastic surgeons.

Results: For 730 men with Dupuytren disease, the surgeons' reported prevalence rate of Peyronie disease was 7.8 percent and of Ledderhose disease was 16.1 percent. The participants themselves reported prevalence rates of 8.8 percent for Peyronie disease and of 22.0 percent for Ledderhose disease.

Conclusions: In the Dupuytren patient cohort, the prevalence of Peyronie disease was lower than that described in the literature. The prevalence of Ledderhose disease corresponded with the rates from the literature. However, both were underreported by plastic surgeons, which calls for a rise in awareness, recognition, and referral to a urologist when the conditions are bothersome or symptomatic. (*Plast. Reconstr. Surg.* 145: 978, 2020.)

Dupuytren, Peyronie, and Ledderhose diseases are fibroproliferative disorders characterized by abnormal collagen deposition in the palmar fascia of the hand, tunica albuginea of the penis, and plantar fascia of the foot, respectively (Fig. 1). In Dupuytren disease, nodules and cords can form in the connective tissue; the cords can cause debilitating flexion contractures of the digits. In Ledderhose disease, lumps in the sole of the foot can result in pain during walking. In Peyronie disease, plaque formation results in penile pain, shortening, curvature, and loss of rigidity. These diseases are thought to have a similar disease mechanism, and Abernathy (London, United Kingdom) first reported on their relation in 1828.¹

The tunica albuginea is a two-layered structure of inner circular and outer longitudinal layers of

connective tissue encompassing the paired corpora cavernosa. An incomplete septum separates the corpora and anchors dorsally from the circular inner layer of the tunica albuginea. Erection and bending of the rigid corpora cavernosa may lead to delamination at this location (Fig. 2). In practice, this means that more than 95 percent of the fibrotic "plaques" are located on the dorsal site of the penis. Similarly, the ulnar metacarpals are more mobile than those at the radial site and are likely to be more vulnerable to tensile stress. The same is true for the distal medial border of the footpad, which is the typical location of Ledderhose disease.

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Fig. 1. Abnormal collagen deposition in the palmar fascia of the hand, tunica albuginea of the penis, and the plantar fascia of the foot leading to Dupuytren, Peyronie, and Ledderhose diseases, respectively.

Fig. 2. (Left) Penile cross-section(left). (Right) The mechanism of trauma in the magnified vulnerable region. (I) The tunica albuginea is a two-layered structure of inner circular and outer longitudinal layers of connective tissue encompassing the paired corpora cavernosa. An incomplete septum separates the corpora and anchors dorsally from the circular inner layer of the tunica. (II) Erection and bending of the rigid corpora cavernosa may lead to elastic tissue fatigue, subsequent ruptures, and scar tissue. Persistent tension may lead to delamination of tunica albuginea layers, which fill with clots and turn into plaque in individuals susceptible to Peyronie disease.

In the 1960s, it was suggested that patients with Peyronie disease had intercourse more frequently and more vigorously than age-matched cohorts, but in scientific practice it was impossible to prove this.² However, there is no question that an accident during penetration when the penis bends excessively may induce Peyronie disease.

More recently, it was shown that the disorders have a familial aggregation, and several genetic risk variants are known to be associated. In 2012, our research group associated nine loci to Dupuytren disease in the first genome-wide association study of Dupuytren disease, and one of these nine loci could also be associated with Peyronie disease.^{3,4} Nowadays, there are 26 known risk variants for Dupuytren

disease, providing possibilities to further explore its genetic correlation with Peyronie disease. In 2004, Qian et al.⁵ had already demonstrated that the patterns of gene expression alteration of certain genes in Dupuytren disease and Peyronie disease were similar, indicating a common pathophysiology.

Dupuytren disease, Peyronie disease, and Ledderhose disease predominantly present in older men, and trauma seems to play a significant role. Interestingly, 51.7 percent of 169 Dutch field hockey players more than 65 years old had Dupuytren disease (controls, 13.8 percent).⁶ Also, with regard to Peyronie disease, trauma to the tunica albuginea combined with a genetic susceptibility is the most widely accepted etiological hypothesis.⁷ The contracture characteristic of Dupuytren disease and Peyronie disease appears to bear a relationship to the distribution of stress in the palmar fascia and the tunica albuginea of the corpora cavernosa.⁸ Age-related loss of tissue elasticity renders both structures susceptible to peaks of tensile stress. Biological cell studies have identified overlap in patterns of chromosomal aberrations in fibroblasts from Peyronie disease and Dupuytren disease lesions.⁹

Concurrent prevalences of Ledderhose disease and Dupuytren disease have been described by several authors in small to moderate sample sizes.^{10–15} Coinciding prevalences of Peyronie disease in Dupuytren disease, however, have only been described twice: in preliminary results by Dolmans et al.⁴ in a sample of 361 patients, and recently by Shindel et al.¹⁶ in a sample of 85 patients. Since 2007, we have been gathering the clinical information of patients with Dupuytren disease, Peyronie disease, and Ledderhose disease. We report Peyronie disease and Ledderhose disease prevalences in the largest sample size to date, consisting of 730 patients with Dupuytren disease, to update our knowledge of prevalence rates and to create awareness. We also present doctor- and patient (self)-reported prevalences separately to provide insight into the rate of reporting, because Peyronie disease is known to be underreported because of embarrassment. Because many patients with Peyronie disease feel ashamed to talk about their condition, we reflect on the possible role of plastic and hand surgeons with regard to counseling their patients with Dupuytren disease about possible concomitant Peyronie disease.

METHODS

Ethical Approval

Approval for the Genetic Origin of Dupuytren Disease and Associated Fibromatosis (GODDAF)

study was acquired from the Medical Ethics Committee 2007/067 of the University Medical Center Groningen. All participants provided written informed consent.

Data and Collection

The Genetic Origin of Dupuytren Disease and Associated Fibromatosis database contains patients affected by Dupuytren disease and/or Peyronie disease and/or Ledderhose disease. The participants were recruited from 2007 to 2016 from the outpatient clinics for plastic surgery of several hospitals in the northern part of the Netherlands and from the Department of Urology of the University Hospital in Groningen. For this study, we used only patients recruited from the outpatient clinics for plastic surgery. Dupuytren disease was diagnosed by surgeons through physical examination. The database contains questionnaires completed by surgeons and patients describing patient characteristics, demographics, diathesis factors, and the extent of the fibroproliferative disorder(s). Data on surgeon-reported concomitant Ledderhose disease and Peyronie disease in patients with Dupuytren disease were gathered during history taking. Patient-reported concomitant Ledderhose disease and Peyronie disease were verified with questionnaires. (See **Appendix, Supplemental Digital Content 1**, which shows the doctor questionnaire, <http://links.lww.com/PRS/E9>, and **Appendix, Supplemental Digital Content 2**, which shows the patient questionnaire, <http://links.lww.com/PRS/E10>.) Patients who answered “I think so” (**Appendix, Supplemental Digital Content 2**) to whether or not they had concomitant Peyronie disease or Ledderhose disease were part of the “yes” group in the data analysis.

Statistics

Descriptive statistics for continuous data on interval or ratio level of measurement are presented using means and standard deviations, and nominal data are presented as frequencies and percentages. We used chi-square tests to control for allergies, alcohol consumption, and smoking.

RESULTS

Our total cohort of 1725 patients with Dupuytren disease consisted of 1307 men (75.8 percent) and 415 women (24.1 percent). For three patients (1 percent), data on sex were missing. The mean patient age was 70.1 years (SD, 10.7 years). Ninety-four percent were white. Allergies, alcohol consumption, and smoking did not significantly differ among groups.

Fig. 3. (Left) Doctor-reported and (right) patient-reported Peyronie disease (PD).

Peyronie Disease in Patients with Dupuytren Disease

Peyronie disease was determined by questionnaires completed at the start of the study by both the participant and the surgeon. There were no patients referred by urologists. For 730 of the 1307 male patients with Dupuytren disease, doctor-reported data on Peyronie disease were available (577 missing). In 57 of these 730 male patients, the surgeon noted the presence of Peyronie disease, indicating a prevalence rate of 7.8 percent (Fig. 3, left). According to the patients themselves, Peyronie disease was present in 102 of 1163 (8.8 percent). Fifty of the 1307 patients indicated they did not know whether they had Peyronie disease, and for 94 patients, data were missing (Fig. 3, right).

Ledderhose Disease in Patients with Dupuytren Disease

For 619 of the 1725 patients, surgeons' data on Ledderhose disease were missing. They reported the presence of Ledderhose disease in 178 of the remaining 1106 Dupuytren disease cases, indicating a prevalence of 16.1 percent (Fig. 4, left). According to the patients' reports ($n = 1539$), Ledderhose disease was present in 338 of them (24.0 percent). Sixty-nine indicated they did not know whether they had Ledderhose disease, and for 117 patients, data were missing (Fig. 4, right).

DISCUSSION

Dupuytren, Peyronie, and Ledderhose diseases are common disorders in white people of northwestern European origin.⁹ In other parts of

Fig. 4. (Left) Doctor-reported and (right) patient-reported Ledderhose disease (LD).

Table 1. Prevalence of Ledderhose Disease in Patients with Dupuytren Disease

Authors	Year	Total (n)	LD	(%)
Allen et al. ¹⁰	1955	Unknown	Unknown	9.0
Gordon ¹¹	1964	101	9	8.9
Hueston ¹²	1972	159	19	12.0
Caroli et al. ¹³	1991	352	Unknown	6.0
Brenner et al. ¹⁴	2001	566	21	3.7
De Greef and De Smet ¹⁸	2008	65	12	19.0
Gudmundsson et al. ¹⁵	2012	137	18	13.2
Dolmans et al. ⁴	2012	475	72	13
Schurer et al. ¹⁹	2016	2235	624	30
Shindel et al. ¹⁶	2017	85	9	10.6
Present study	2019	1106	SR 78	16.1
		1539	PR 338	22.0

LD, Ledderhose disease; PR, patient reported; SR, surgeon reported.

Table 2. Prevalence of Peyronie Disease in Patients with Dupuytren Disease

Authors	Year	Total (n)	PD	(%)
Dolmans et al. ⁴	2012	361	22	6.4
Shindel et al. ¹⁶	2017	85	22	26
Present study	2019	730	Surg 57	7.8
		1163	Pts 102	8.8

PD, Peyronie disease; Pts, patients; Surg, surgeons.

the world, they are regarded as much less common.¹⁷ In this article, we describe, as far as we know, one of a few scientific reports that deal with the prevalence of Ledderhose disease in patients with Dupuytren disease and one of even fewer that report on the prevalence of Peyronie disease in a population of men with Dupuytren disease (Tables 1 and 2). With a much larger sample size than previous studies,¹⁰ we updated the concurrent prevalences of Peyronie disease and Ledderhose disease in patients with Dupuytren disease, subdivided into surgeon- and patient-reported prevalence, which is a novelty compared with previous studies. Because the present study is an update of our previous research, by Dolmans et al.,⁴ these samples partially overlap.

Ledderhose Disease

A systematic review and meta-analysis in the general population of Western countries showed a Ledderhose disease prevalence rate of 1.4 percent.¹⁷ In the preliminary analysis by Dolmans et al. of our cohort of patients affected by Dupuytren disease, we found a surgeon-reported Ledderhose disease prevalence of 13 percent.⁸ In the present study, we found Ledderhose disease prevalence rates of 16.1 percent respectively 22.0 percent. These rates are similar to and confirm percentages found in Flanders, Belgium.¹⁸ Patient-reported data gathered by Schurer et al.¹⁹ for the

International Dupuytren Society showed a higher percentage (30 percent) in a large population. Differences may be explained by the use of questionnaires and the uncertain diagnosis. Lumps on the sole of the foot can have many other causes than Ledderhose disease.²⁰

Peyronie Disease

A recent study from California hypothesized that the prevalence of Peyronie disease in patients with Dupuytren disease would be similar (i.e., approximately 22 percent) to the rate found previously in 415 consecutive patients with Peyronie disease in the northern part of the Netherlands.²¹ Remarkably, the California study found that the prevalence of Peyronie disease in 85 men with Dupuytren disease was as high as 26 percent, as opposed to the rate found in the present study (Table 2).¹⁶ One explanation could be that, in the Californian patients, the Dupuytren disease may have been more severe and, for that reason, showed a higher Peyronie disease prevalence rate. In addition, the Californian group reported the prevalence of Peyronie disease as the percentage of patients experiencing “Peyronie disease–like symptoms,” possibly causing an overestimation of prevalence of the actual disease.

In the general male population, Peyronie disease prevalence rates vary between 3 percent and 9 percent, with a median age of onset of 53 years.²² The incidence of the disease appears to be increasing, which is likely not the case in absolute figures, but indeed relatively and because of the availability of phosphodiesterase type 5 inhibitors [erectile dysfunction pills such as Viagra (sildenafil); Pfizer, Karlsruhe, Germany] for men with somatic erectile dysfunction, who would otherwise have been unaware of their penile curvature. Furthermore, the Peyronie disease prevalence is commonly underreported because of the sensitivity of the topic.²³ A review on the psychological aspects of Peyronie disease suggests that as many as 81 percent of patients with the disease report emotional difficulties; 48 percent report a clinically meaningful depression (26 percent moderate; 21 percent severe); and 54 percent report relationship problems as the result of the disease.²⁴ Regarding body image and self-esteem, patients with the disease describe themselves in qualitative terms such as “abnormal,” “ugly,” “disgusting,” “like a cripple,” and a “half man,” and some of them mention feelings of shame.²⁵ Many express a loss of sexual confidence and decreased sexual interest, and feel a sense of stigmatization

T1,T2

and isolation leading to difficulties in speaking about their disease with sexual partners. Physicians should actively ask whether or not this is the case and provide solutions or help. Referral to a urologist to investigate medical (im)possibilities may be an outcome. Psychological support must be considered, keeping in mind an empathic attitude, and referral to a psychologist should always be considered.

There are no data on the possible psychological effects of Ledderhose disease. We identified only one study about the indirect psychological effects of Dupuytren disease on alcohol consumption and smoking.²⁶ With our aging population and the increasing retirement age, Dupuytren disease poses a growing threat to one's capacity to work and thus the economy, and is likely to have a psychological burden. However, Dupuytren disease and Ledderhose disease probably do not impair partner relationships and self-confidence in the way Peyronie disease does.²⁷

Limitations of This Study

A limitation of prevalence research in general is the heterogeneity in appearance of Dupuytren disease, Peyronie disease, and Ledderhose disease, and thus their diagnosis. Because these are progressive diseases, the full extent of all three disorders may not have been present at the first presentation, when the questionnaires were filled out. Furthermore, some studies present doctor-reported data and others present patient-reported data or "disease-like" symptoms. We differentiated between disease reported by patients and by surgeons, and concluded that a substantial number of patients did not report the presence of Peyronie disease to the hand surgeon, probably because of embarrassment. We acknowledge that the identification of disease through history taking, rather than confirmation on physical examination, may introduce an element of either overreporting or underreporting. In general, a patient may misinterpret symptoms when reporting Peyronie disease and Ledderhose disease; thus, meaningful data on self-reported disease require surveys with an explicit description, such as "curvature of the penis during erection," rather than simply asking whether the patient has ever had Peyronie or Ledderhose disease.

As a result of the retrospective analysis of the data for this research, many questionnaires were unfortunately missing. Still, compared with other studies, our sample size is large. In addition, all participants originated from the same geographical location, making effect modification

by genetic variability less likely. Undoubtedly, the men in our Dupuytren disease cohort were more severely affected than men in the general population. Prevalence rates, therefore, may be higher in our cohort than in the general population, as a more severe Dupuytren disease course is associated with increased Peyronie disease and Ledderhose disease/ectopic disease prevalence rates.^{28–30} This patient population, however, comprises the population presenting itself at the outpatient clinics, and thus is relevant to hand surgeons.

For urologists, it is a small effort to palpate the palmar fascia of the hands of patients with Peyronie disease, and they therefore generally consider this examination as part of the routine examination at the first visit.⁵ Understandably, plastic surgeons will be reluctant to examine the penis of their patients with Dupuytren disease, because it is time consuming and can be uncomfortable.

However, more than Dupuytren disease and Ledderhose disease, Peyronie disease can have devastating psychological consequences. Peyronie disease is often associated with erectile dysfunction and can therefore also have a negative impact on the well-being of the sexual partner. In daily life, most patients with Peyronie disease feel embarrassed to report their sexual complaints. This raises the question of whether plastic surgeons need to actively ask their patients with Dupuytren disease for symptoms of Peyronie disease. In our opinion, they do not have to go into detail, but they can propose a referral to a competent urologist.

CONCLUSIONS

Dupuytren disease, Peyronie disease, and Ledderhose disease are very common disorders and very likely share (at least in part) a similar disease mechanism and overlapping genetic risk factors. In our Dupuytren disease patient cohort, the prevalence of Peyronie disease was lower than that described in the literature. The prevalence of Ledderhose disease corresponded with the rates from the literature. However, both were underreported by plastic surgeons, calling for a rise in awareness, recognition, and referral to a urologist when the conditions are bothersome or symptomatic.

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