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The prevalence of Dupuytren contractures in patients with psoriasis

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Summary

Background. Dupuytren contracture (DC) is a fibrocontractile disease of the palms, affecting approximately 4% of the population, while psoriasis is an immune-mediated disease, affecting 2% of the population. Through clinical observation in our psoriasis clinic, we found an apparent increased prevalence of DC in patients with psoriasis compared with the general population. This has not previously been statistically verified in a clinical study.

Aim. To evaluate the prevalence of DC in the full range of clinical psoriasis phenotypes.

Methods. In total, 98 patients with psoriasis attending our psoriasis clinic were examined for DC, based on predetermined criteria. In addition, 84 patients with DC, obtained from a specialist hand clinic, were assessed using a validated psoriasis questionnaire. We utilized Bayes theorem and bootstrap simulation to calculate the conditional prevalence of DC, then we used the results to compare the prevalence of DC between patients with psoriasis and a nonpsoriasis population.

Results. The percentage of patients with DC was 19.6% in the psoriasis population and 3.6% in the nonpsoriasis population. Development of DC showed a phenotypic predilection, with 39.1% of patients with predominantly palmoplantar involvement and 38.9% of patients with intertriginous psoriasis developing DC compared with 12.7% of patients with psoriasis who did not have these two phenotypical presentations.

Conclusions. Our data show a positive correlation between psoriasis and DC. Patients with the palmoplantar phenotype of psoriasis were more likely to develop DC. By understanding this relationship, dermatologists may diagnose DC early in its onset in patients with psoriasis, prompting referral to hand surgeons when appropriate.

Introduction

Psoriasis is a systemic, immune-mediated, genetic disease, presenting clinically as sharply demarcated, scaly erythematous plaques and affecting up to 2% of the world's population.[1] It is is a T cell-mediated disease associated with an abnormal proliferation and differentiation of epidermal keratinocytes, secondary to activation of Th1 and Th17 cells.[2,3] Psoriasis was formerly believed to be a condition purely confined to the skin, but accumulating evidence supports associations with multiple systemic disorders. To date, 11 associations

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have been statistically validated, and include psoriatic arthritis, cardiovascular disease, Crohn disease, diabetes mellitus, metabolic syndrome and nonalcoholic fatty liver disease.[4]

Dupuytren contracture (DC) is a benign fibromatosis of the fingers, occurring as a result of thickening and contracture of the connective tissues of the palm and fingers.[5] The ratio of collagen type I to type III is increased significantly in DC, leading to thickening of the palmar fascia. Because collagen III is considerably thicker than collagen I, thickening and tension form on the palmar fascia, resulting in the formation of single or multiple nodules around the palmar fascia. This can lead to a fixed flexion deformity of the metacarpophalangeal and proximal interphalangeal joints, resulting in a permanently contracted position, which impairs quality of life.[6] While the cause of this disease is unknown, known risk factors for DC include diabetes, epilepsy and alcoholism.[7]

Through clinical observation of our psoriasis population, we observed an apparent increased prevalence of DC and/or nodules in patients with psoriasis compared with the general population. This has not previously been verified in a well-designed, statistically verified, prospective clinical study. Thus, the objective of this study was to evaluate the prevalence of DC in patients with psoriasis, and to determine if the development of DC is associated with particular psoriasis clinical phenotypes.

Methods

The study protocol was approved by the IRB on human experimentation at Baylor Healthcare System (BHCS), and all patients provided written informed consent.

To determine the prevalence of DC in patients with psoriasis, we examined 98 consecutive patients with a diagnosis of psoriasis in our psoriasis referral clinic. Clinical evaluation of DC was performed by an orthopaedic hand surgeon specializing in the management of DC, based on predetermined diagnostic criteria.

In the second part of the study, we assessed the prevalence of psoriasis in 84 patients with a diagnosis of DC, recruited from the orthopaedic hand specialist clinic. Psoriasis in these patients was assessed by dermatologists using a validated, standardized psoriasis phenotype questionnaire.

The prevalence of the two diseases found in this observational study of both clinics and their prevalence in the general US population were used to compare the probability of developing DC based on the presence or absence of psoriasis.

Statistical analysis

The distribution of the difference in probability of developing DC, depending on the presence or absence of psoriasis, was first estimated using the data from both clinics and utilizing Bayes theorem using a range of possible population prevalence for psoriasis (0.5–2.5%) and a population prevalence of 4% for DC. For the descriptive statistics, the mean, standard deviation and median for the continuous variables, and the frequency and percentage for the categorical variables were used to assess the probability.

For the analysis, a Z-test approximation for binomial was used to evaluate the difference between two proportions. To determine the appropriate standard deviation to use in the Z-test, a bootstrap simulation was performed. The bootstrap method builds a distribution by resampling the given data with replacements multiple times, each time calculating the difference in the probability of developing DC within the psoriasis population and the nonpsoriasis population. The standard deviation of the differences was then calculated, and the significance was obtained based on a one-sided test at the 0.05 level.

R software (v2.14.1; http://www.R-project.org/) was used to analyze the data. The data were entered into a table (Table 1), and the probability of contracting DC was calculated for patients with and without psoriasis.

Results

We first estimated the distribution of the difference in the probability of developing DC depending on the presence or absence of psoriasis (Table 1). A range of possible prevalences for both DC and psoriasis was considered. The prevalence of DC in our cohort of patients with psoriasis was found to be significantly higher than in the nonpsoriasis population (19.6% vs. 3.6%, respectively).

Certain variables assessed in our psoriasis population were also associated with an increased prevalence of DC (Tables 2 and 3). Patients with the palmoplantar phenotype of psoriasis had a significantly higher prevalence of DC compared with patients with other forms (39.1% vs. 12.7%, respectively). Similarly, intertriginous psoriasis had a statistically significant association with development of DC, occurring in 38.9% of patients. Use of systemic medications showed a statistical significance in the development of DC, occurring in 33% of patients receiving systemic treatment; however, use of only methotrexate and biological agents

Table 1 Variables tested for statistical significance in developing DC.

Variable	Developed DC: Yes (n = 19; 19.6%)	Developed DC: No (n = 78; 80.4%)	P
Demographics			
Sex			
Female	12 (26.1)	34 (73.9)	0.13
Male	7 (13.7)	44 (86.3)	
Age, years*	59.1 ± 12.90	49.9 ± 14.98	0.02
Ethnicity			
White	19 (21.3)	70 (78.7)	0.15
Other	0 (0.0)	8 (100.0)	
Tobacco use			
Yes	8 (20.5)	31 (79.5)	0.85
No	11 (19.0)	47 (81.0)	
Alcohol use			
Yes	13 (18.8)	56 (81.2)	0.65
No	6 (23.1)	20 (76.9)	
Family with psoriasis			
Yes	10 (23.3)	33 (76.7)	0.31
No	8 (15.1)	45 (84.9)	
Comorbidities			
Crohn disease			
Yes	0 (0.0)	1 (100.0)	0.63
No	18 (19.4)	75 (80.6)	
Type 1 diabetes			
Yes	0 (0.0)	1 (100.0)	0.63
No	18 (19.4)	75 (80.6)	
Type 2 diabetes			
Yes	3 (30.0)	7 (70.0)	0.35
No	15 (17.6)	70 (82.4)	
Rheumatoid arthritis			
Yes	0 (0.0)	2 (100.0)	0.49
No	18 (19.6)	74 (80.4)	
Lupus			
Yes	0 (0.0)	1 (100.0)	0.63
No	18 (19.4)	75 (80.6)	
Liver disease			
Yes	0 (0.0)	5 (100.0)	0.26
No	19 (20.7)	73 (79.3)	
Thyroid disease			
Yes	5 (41.7)	7 (58.3)	0.03
No	13 (15.9)	69 (84.1)	
Atopic dermatitis			
Yes	0 (0.0)	1 (100.0)	0.62
No	18 (19.4)	75 (80.6)	
High cholesterol			
Yes	8 (22.9)	27 (77.1)	0.46
No	10 (16.7)	50 (83.3)	
Hypertension			
Yes	7 (24.1)	22 (75.9)	0.41
No	11 (16.9)	54 (83.1)	
CAD			
Yes	1 (20.0)	4 (80.0)	0.96
No	17 (19.1)	72 (80.9)	
Stroke			
Yes	0 (0.0)	1 (100.0)	0.63
No	18 (19.4)	75 (80.6)	
Psoriasis: diagnosis			
Duration of the disease, years*	24.3 ± 19.58	22.2 ± 15.00	0.62
Age psoriasis diagnosed, years*	41.3 ± 19.57	30.2 ± 14.91	0.01
Age PsA diagnosed, years*	50.6 ± 11.18	34.6 ± 9.96	0.00
BSA			
Mild (< 5%)	13 (17.1)	63 (82.9)	0.04
Moderate (5–10%)	1 (10.0)	9 (90.0)	
Severe (≥ 10%)	5 (50.0)	5 (50.0)	
Chronic plaque psoriasis			
Yes	19 (20.2)	75 (79.8)	0.39
No	0 (0.0)	3 (100.0)	
Intertriginous psoriasis			
Yes	7 (38.9)	11 (61.1)	0.02
No	11 (14.5)	65 (85.5)	
Palmoplantar psoriasis			
Yes	9 (39.1)	14 (60.9)	0.01
No	9 (12.7)	62 (87.3)	
Nail psoriasis			
Yes	11 (25.6)	32 (74.4)	0.12
No	7 (13.2)	46 (86.8)	
Pustular psoriasis			
No	15 (17.6)	70 (82.4)	0.22
Generalized	0 (0.0)	1 (100.0)	
Palmoplantar	4 (40.0)	6 (60.0)	
Psoriasis: medications			
Methotrexate			
Yes	6 (37.5)	10 (62.5)	0.05
No	13 (16.0)	68 (84.0)	
Topical therapy			
Yes	19 (21.8)	68 (78.2)	0.20
No	0 (0.0)	10 (100.0)	
Phototherapy			
Yes	19 (20.0)	76 (80.0)	0.10
No	0 (0.0)	2 (100.0)	
Systemic therapy			
Yes	10 (33.3)	20 (66.7)	0.02
No	9 (13.4)	58 (86.6)	
Biological therapy			
Yes	6 (13.0)	40 (87.0)	0.12
No	13 (25.5)	38 (74.5)	

BSA, body surface area; CAD, coronary artery disease; DC, Dupuytren contracture; PsA, psoriatic arthritis. Data are n (%) unless otherwise stated. *Mean ± SD.

did not have an effect on the development or improvement of DC. Lastly, within the psoriasis cohort, there was a statistically significant association between the development or improvement of DC and the age of diagnosis of psoriatic arthritis, with patients developing

Table 2 Variables tested for statistical significance in developing psoriasis.

Variable	Developed psoriasis: Yes (n = 10; 11.9%)	Developed psoriasis: No (n = 74; 88.1%)	P
Demographics			
Sex			
Female	5 (12.5)	35 (87.5)	0.87
Male	5 (11.4)	39 (88.6)	
Age, years*	64.6 ± 5.25	64.1 ± 10.37	0.88
Age at onset of palmar nodules, years*	53.7 ± 7.97	51.1 ± 12.80	0.53
Ethnicity			
White	10 (12.4)	71 (87.6)	0.10
Other	0 (0.0)	3 (100.0)	
Tobacco use			
Yes	1 (14.3)	6 (85.7)	0.84
No	9 (11.7)	68 (88.3)	
Alcohol use			
Yes	8 (13.3)	52 (86.7)	0.52
No	2 (8.3)	22 (91.7)	
Comorbidities			
High blood pressure			
No	4 (18.2)	18 (81.8)	0.16
Personal history	1 (5.0)	19 (95.0)	
Family history	1 (4.5)	21 (95.5)	
Both personal and family history	4 (25.0)	12 (75.0)	
Myocardial infarction			
No	8 (15.1)	45 (84.9)	0.38
Family history	1 (6.3)	15 (93.8)	
Congestive heart failure			
No	6 (10.7)	50 (89.3)	0.44
Personal history	0 (0.0)	2 (100.0)	
Family history	3 (27.3)	8 (72.7)	
Both personal and family history	0 (0.0)	1 (100.0)	
Liver disease			
No	8 (12.9)	54 (87.1)	0.77
Personal history	0 (0.0)	2 (100.0)	
Family history	1 (20.0)	4 (80.0)	
Thyroid disease			
No	7 (13.0)	47 (87.0)	0.68
Personal history	2 (25.0)	6 (75.0)	
Family history	0 (0.0)	3 (100.0)	
Both personal and family history	0 (0.0)	1 (100.0)	
Crohn disease			
No	8 (12.3)	57 (87.7)	0.03
Personal history	0 (0.0)	2 (100.0)	
Family history	1 (100.0)	0 (0.0)	
Type 1 diabetes			
No	9 (14.5)	53 (85.5)	0.80
Personal history	0 (0.0)	1 (100.0)	
Family history	0 (0.0)	4 (100.0)	
Both personal and family history	0 (0.0)	1 (100.0)	
Type 2 diabetes			
No	7 (13.7)	44 (86.3)	0.79
Personal history	0 (0.0)	3 (100.0)	
Family history	1 (7.7)	12 (92.3)	
Both personal and family history	1 (20.0)	4 (80.0)	
High cholesterol			
No	3 (10.3)	26 (89.7)	0.90
Personal history	4 (16.0)	21 (84.0)	
Family history	1 (9.1)	10 (90.9)	
Both personal and family history	1 (10.0)	9 (90.0)	
Multiple sclerosis	1 (6.3)	15 (93.8)	0.4
No	9 (14.1)	55 (85.9)	
Family history	0 (0.0)	4 (100.0)	
Psoriatic arthritis			
No	7 (11.1)	56 (88.9)	0.03
Personal history	0 (0.0)	1 (100.0)	
Family history	1 (50.0)	1 (50.0)	
Both personal and family history	1 (100.0)	0 (0.0)	
Epilepsy			
No	9 (13.6)	57 (86.4)	0.69
Family history	0 (0.0)	1 (100.0)	
Carpal tunnel syndrome			
No	9 (14.8)	52 (85.2)	0.51
Personal history	0 (0.0)	3 (100.0)	
Family history	0 (0.0)	5 (100.0)	
DC: diagnosis			
History of manual labour			
Yes	3 (11.1)	24 (88.9)	0.65
No	6 (15.0)	34 (85.0)	
History of hand trauma			
Yes	1 (6.7)	14 (93.3)	0.33
No	8 (16.7)	40 (83.3)	
History of surgery or radiation			
Yes	4 (10.5)	34 (89.5)	0.36
No	6 (18.2)	27 (81.8)	
Stage, left hand			0.76
0	2 (11.8)	15 (88.2)	
1	2 (10.0)	18 (90.0)	
2	2 (28.6)	5 (71.4)	
3	0 (0.0)	4 (100.0)	
4	0 (0.0)	1 (100.0)	
N			
Stage, right hand	0 (0.0)	8 (100.0)	0.59
0	1 (11.1)	8 (88.9)	
1	2 (7.4)	25 (92.6)	
2	3 (27.3)	8 (72.7)	
3	0 (0.0)	4 (100.0)	
4	0 (0.0)	1 (100.0)	
N	4 (16.7)	20 (83.3)	

DC, Dupytren contracture. Data are n (%) unless otherwise stated. *Mean ± SD.

Table 3 Patients who developed psoriasis.

Variable	
Total BSA*	0.12 ± 0.33
Age at onset of psoriasis, years*	45.1 ± 18.14
Chronic plaque psoriasis	
Yes	6 (60.0)
No	4 (40.0)
Intertriginous psoriasis	
Yes	3 (30.0)
No	7 (70.0)
Palmoplantar psoriasis	
Yes	2 (20.0)
No	8 (80.0)
Nail psoriasis	
Yes	1 (10.0)
No	9 (90.0)

BSA, body surface area; Data are *n* (%) unless otherwise stated. *Mean ± SD.

psoriatic arthritis at an older age being more likely to develop DC. Other variables tested for were alcohol, tobacco usage, and comorbidities such as type II diabetes, CVA, coronary artery disease, and high cholesterol, but none of these was found to be statistically associated with DC.

Discussion

Based on the data obtained from our study, it can be concluded that there is a statistically significant correlation between DC and psoriasis versus the general population.

The association between these two conditions may be related to the presence of platelet-derived growth factor (PDGF) receptors in both psoriasis and DC.[8] The development of DC is biologically similar to wound repair, with growth factors playing an important role in the pathophysiology of this disease. PDGF is a required element for cell division of fibroblasts, and is known to stimulate proliferation of connective tissue. A study conducted by Terek *et al.* found that PDGF was typically found in healing wounds, and was also present in increased levels in the proliferative and involutional stages of DC. They examined six tissue samples from patients with DC, using immunohistochemistry with 5B5 antibody, a marker for fibroblasts, and compared them with tissue from normal fascia. Southern blotting and *in situ* hybridization showed that the *PDGF-B* gene was expressed at higher concentrations in all six specimens from patients with DC compared with tissue from normal fascia. Thus, PDGF receptors appear to play an important role in the aetiology of DC and in the formation of DC nodules around tendons, owing to their ability to stimulate the proliferation of myofibroblasts.[9]

Similarly, psoriatic lesions also show increased expression of PDGF, as cultured psoriatic fibroblasts are more responsive to the chemotactic and mitogenic properties of PDGF. In one study, a western blotting analysis performed on tissue extracts from two patients with psoriasis using PR7212 antibody revealed that the PDGF receptor is expressed at higher levels in psoriatic lesions than in nonpsoriatic lesions.[8]

Moreover, both DC and psoriasis have aberrations in the Wnt signalling pathway, which is known to regulate proliferation and differentiation of fibroblasts. The *Wnt* gene family consists of genes that are able to encode glycoproteins and extracellular signalling molecules. A study conducted by Dolmans *et al.*[10] demonstrated four DC genes that encoded proteins present in the Wnt signalling pathway. These encoded Wnt proteins were bound to Frizzled receptors, eventually leading to a decrease in the rate of β-catenin degradation and therefore a higher level of β-catenin;[10] such an increased level of β-catenin suggests that the Wnt signalling pathway is overstimulated in DC. Increased activity of *Wnt* genes stimulates Wnt signalling and results in reduced β-catenin degradation. This in turn causes a proliferation of fibroblasts, ultimately leading to the development of DC.[11]

Similarly the Wnt signalling proteins are important mediators in psoriasis. In a study conducted by Gudjonsson *et al.*, biopsy samples of psoriatic skin were found to have a significant change in the amount of activity of the Wnt signalling pathways and an aberration of the levels of Wnt proteins compared with normal skin.[12]

In the current study, we found several variables had an association with the development of DC, including increased body surface area (BSA), use of systemic agents, palmoplantar psoriasis, intertriginous psoriasis, and the development of psoriatic arthritis at an older age. Increased prevalence of DC in patients with palmoplantar psoriasis may be due to an increase in PDGF receptors in the palms and soles. Once PDGF becomes elevated, the likelihood of developing DC increases, as PDGF receptors have a direct relationship with the development of fibroblasts and in turn, the development of nodules.[13] The use of systemic agents, such as methotrexate and ciclosporin, for the treatment of psoriasis appeared to be associated with an increased risk of DC in the psoriasis population, suggesting either an association with more widespread psoriatic disease or an effect caused by the immunosuppressant properties of these systemic agents.

Although no statistically significant correlation between methotrexate and DC was found in our study, methotrexate is associated with profibrotic properties in the liver.[14] Additionally, although we did not control for ciclosporin use in our study, ciclosporin actually reduces both PDGF-AA and PDGF-Rα expression in intimal cells,[15] thus, initiation of ciclosporin may affect the levels of PDGF receptors, and in turn, reduce the development of DC.

It is important to recognize these variables because currently there are no known interventional guidelines to prevent DC. In recognizing this statistically significant correlation between psoriasis and DC contractures, dermatologists may potentially be able to prevent the development of DC by appropriate screening for this condition, prompting immediate referral to hand surgeons, and thereby reducing the potential for flexion deformities, contractures and permanent disability. Furthermore, the potential for gene analysis of patients with psoriasis and DC may reveal a specific linkage between these two common conditions. One omission from our study was our inability to evaluate Peyronie's disease in the two patient populations, as the condition is known to be associated with DC.

What's already known about this topic?

- Psoriasis is known to be associated with a range of systemic disorders.
- DC is a rare disease, affecting 4% of the population.

What does this study add?

- Through clinical observation in our psoriasis specialty clinic we observed an apparent increased incidence of DC in patients with psoriasis compared with the general population.
- This has not previously been verified in a clinical study.
- By understanding this relationship, dermatologists can play an important role in diagnosing DC in *their* patients with psoriasis early in its onset, prompting referral to hand surgeons.

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