

# Evaluation of Dupuytren's Disease Risk Factors and Familial Risk Quantification for Receiving a Diagnosis and Undergoing Treatment: A Population-Based Epidemiological Analysis

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**INTRODUCTION:** Genetic, environmental, and physiological factors have been implicated in the pathogenesis of Dupuytren's disease (DD). However, the literature – mostly based upon small study populations – is conflicting in regard to many of the proposed non-genetic physiological risk factors. Although DD may be inherited in an autosomal-dominant fashion with variable penetrance, we currently are unable to counsel patients in regard to their increased likelihood of receiving a DD diagnosis, or increased likelihood of undergoing DD treatment, based on having affected family members of various levels of relatedness. Our purpose was to 1) evaluate physiological risk factors for DD, and 2) quantify familial risk of receiving a diagnosis or undergoing treatment for DD, in a population-based cohort.

**METHODS:** Patients diagnosed with, and treated for, DD were identified in the Utah Population Database (UPDB) using related ICD-9/10 and CPT codes. The UPDB contains >8 million individuals in multigenerational pedigrees dating back to the late 1700's which are linked to >30 million medical records. DD patients were mapped to pedigrees to identify high-risk families with an increased incidence of DD diagnosis, or increased incidence of DD treatment (surgical fasciectomy, needle aponeurotomy, or collagenase treatment) relative to control pedigrees. The magnitude of risk for DD diagnosis and DD treatment was separately quantified using relative risks from Cox regression.

**RESULTS:** We included 9579 affected individuals and 44856 controls. Risk quantification for DD diagnosis, and DD treatment, is provided in Table 1. The strongest physiological risk factors for undergoing DD treatment were a personal history of knuckle pads (OR 27.7), Caucasian race (OR 3.44 [inverse of 0.29]), and Hispanic ethnicity (OR 2.1 [inverse of 0.48]). Obesity was confirmed to be protective against DD diagnosis (OR 0.88) and treatment (OR 0.80).

Increasing levels of familial DD involvement were also significantly associated with the risk of DD diagnosis and treatment (Table 2). Notably, having a first-degree relative with DD increased the risk of diagnosis (OR 3.4 to 7.4) and undergoing treatment (OR 4.9 to 14.9) compared to individuals with no family history.

**DISCUSSION:** We identified physiological risk and protective factors associated with DD diagnosis in a large statewide database, many of which were also associated with the risk of undergoing DD treatment. The risk of DD diagnosis and undergoing DD treatment increases relative to familial involvement. Sequencing of the highest risk families is underway to further elucidate the pathophysiology and genetics of aggressive forms of DD.

**SIGNIFICANCE:** These findings have implications for patient counseling and monitoring those at high risk.

**Table 1 - Risk Factor Analysis for Dupuytren's Disease**

Variable	Risk of <b>Diagnosis</b>			Risk of <b>Undergoing Treatment</b>		
	Odds Ratio (OR)	OR 95% CI	p-value	Odds Ratio (OR)	OR 95% CI	p-value
<b>Demographic Variables</b>						
Caucasian (no vs yes) (unknown vs yes)	0.36 2.18	0.31, 0.42 1.87, 2.54	<0.001 <0.001	0.29 4.37	0.22, 0.39 3.50, 5.46	<0.001 <0.001
Hispanic (yes vs no) (unknown vs no)	0.52 0.68	0.47, 0.58 0.60, 0.77	<0.001 <0.001	0.48 0.58	0.40, 0.58 0.47, 0.71	<0.001 <0.001
<b>Proposed Medical Risk Factors</b>						
Alcohol use disorder (yes vs no)	1.27	1.14, 1.40	<0.001	1.44	1.23, 1.69	<0.001
Cirrhosis/liver disease (yes vs no)	1.07	1.00, 1.15	0.06	0.95	0.84, 1.07	0.39
Diabetes (yes vs no)	1.20	1.14, 1.27	<0.001	1.07	0.98, 1.17	0.12
Epilepsy (yes vs no)	1.13	1.00, 1.27	0.04	1.23	1.02, 1.49	0.03
HIV (yes vs nos)	0.95	0.58, 1.56	0.85	0.68	0.26, 1.79	0.44
Obesity (yes vs no)	0.88	0.82, 0.94	<0.001	0.80	0.73, 0.88	<0.001
Psoriasis or psoriatic arthritis (yes vs no)	1.23	1.05, 1.43	0.01	0.75	0.55, 1.01	0.06
Rheumatoid arthritis (yes vs no)	1.30	1.16, 1.44	<0.001	0.88	0.72, 1.07	0.20
Tobacco use (yes vs no)	1.20	1.14, 1.26	<0.001	1.25	1.15, 1.35	<0.001
<b>Ectopic Fibroproliferative Involvement</b>						
Peyronie's disease (yes vs no)	4.02	3.03, 5.34	<0.001	1.88	1.10, 3.23	0.02
Plantar fibromatosis (yes vs no)	1.96	1.80, 2.14	<0.001	1.54	1.32, 1.79	<0.001
Knuckle pads (yes vs no)	15.90	10.8, 23.5	<0.001	27.70	15.9, 48.2	<0.001

**Table 2 - Dupuytren's Risk by Level of Familial Involvement**

Level of Familial Involvement			Risk of <b>Diagnosis</b>			Risk of <b>Undergoing Treatment</b>		
FDR	SDR	TDR	OR	OR 95% CI	p-value	Odds Ratio (OR)	OR 95% CI	p-value
No	No	No	—	—	—	—	—	—
No	No	Yes	1.22	1.10, 1.35	<0.001	1.61	1.32, 1.96	<0.001
No	Yes	No	1.44	1.22, 1.70	<0.001	2.29	1.69, 3.11	<0.001
No	Yes	Yes	2.33	1.69, 3.20	<0.001	3.12	1.37, 7.12	0.01
Yes	No	No	3.43	2.97, 3.94	<0.001	7.30	5.54, 9.61	<0.001
Yes	No	Yes	3.52	2.50, 4.96	<0.001	14.90	5.30, 41.7	<0.001
Yes	Yes	No	5.40	3.47, 8.41	<0.001	11.20	4.54, 27.7	<0.001
Yes	Yes	Yes	7.44	3.77, 14.7	<0.001	4.85	0.37, 64.1	0.23

Abbreviations: FDR = first-degree relative; SDR = second-degree relative; TDR = third-degree relative