The Risk of Dupuytren Surgery in Obese Individuals

Jacques H. Hacquebord, MD,* Vicki Y. Chiu, MS,† Neil G. Harness, MD‡

Purpose Dupuytren disease is a common benign fibroproliferative disorder causing thickening and shortening of the palmar fascia of the hand. The exact etiology of the disease is unclear but known risk factors such as increased age, male sex, and northern European ethnicity have been established. A link between body mass index (BMI) and Dupuytren disease has not been established previously. The purpose of this study was to test the hypothesis that lower BMI is associated with increased risk for Dupuytren disease diagnosis.

Methods After we obtained institutional review board approval, we performed a retrospective review using an electronic medical record and an administrative database from Kaiser Permanente Southern California to identify all enrolled patients there between 2007 and 2014 who were diagnosed with Dupuytren disease. Basic demographic data including age, sex, ethnicity, and BMI were collected. Bivariate and multivariable logistical regression analyses were performed to evaluate for associations between Dupuytren disease and BMI.

Results A total of 2,049,803 patients aged 18 years and older were enrolled in Kaiser Permanente Southern California from 2007 to 2014. During that period, 14,844 patients were identified as having Dupuytren disease. The data were consistent with well-defined demographic trends in Dupuytren disease, with increased rates seen in males, Caucasians, and patients aged 50 years and older. In the multivariable analysis, when controlling for age, race, and sex, the risk of Dupuytren disease was inversely proportional to BMI.

Conclusions The current study showed that higher BMI is associated with decreased odds of having Dupuytren disease. Further work will be required to determine the cause for the apparent relationship between Dupuytren disease and BMI and whether physiologic factors related to obesity may be protective against the development of Dupuytren disease. (J Hand Surg Am. 2017;42(3):149–155. Copyright © 2017 by the American Society for Surgery of the Hand. All rights reserved.)

Type of study/level of evidence Prognostic II.

Key words BMI, diabetes, Dupuytren surgery, Dupuytren disease, obesity.



D UPUYTREN DISEASE IS A BENIGN fibroproliferative disorder that causes thickening and shortening of the palmar fascia of the hand, first described by Guillaume Dupuytren in 1834.¹ This

From the *Department of Orthopaedic Surgery, New York University, New York, NY; and the †Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena; and the ‡Department of Orthopaedic Surgery, Kraemer Medical Office, Kaiser Permanente Orange County, Anaheim, CA.

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form of fibromatosis can progress over time, leading to flexion contractures of the digits, affecting function and quality of life.² The exact etiology of the disease is unclear, but risk factors such as increased age, male

Corresponding author: Jacques H. Hacquebord, MD, Department of Orthopaedic Surgery, New York University, 530 First Avenue, Skirball, Suite 8U, New York, NY 10016; e-mail: jacques.hacquebord@nyumc.org.

0363-5023/17/4203-0001\$36.00/0 http://dx.doi.org/10.1016/j.jhsa.2016.12.010 sex, and northern European ancestry have been established.^{3–7} Other risk factors such as diabetes, alcohol, trauma, occupation, and phenobarbital use have been proposed but remain controversial.^{3,8}

Although Dupuytren disease is usually considered a disease of older men of northern European descent, recent studies found that this understanding was incomplete because the disease is seen in other populations.^{9–11} Anecdotal clinical observations showed an inverse correlation of obesity and Dupuytren disease diagnosis; however, the relationship of body mass index (BMI) to Dupuytren disease has received little attention in the literature. Gudmundsson et al⁸ found that males with Dupuytren disease had a lower BMI compared with unaffected males. Furthermore, higher mean fasting blood glucose levels were seen in men with Dupuytren disease. Because Dupuytren disease affects a more diverse patient population than previously thought, further studies in this area should be larger and more ethnically inclusive.

The purpose of this study was to investigate the association of Dupuytren disease with diabetes and BMI in a large and ethnically diverse population of over 2 million patients.¹² We hypothesized that the risk of Dupuytren disease would be lower in obese patients (those with high BMI) and that diabetic patients with high hemoglobin A1C levels would be at greater risk for the disease compared with patients with better diabetic control.

MATERIALS AND METHODS

After we obtained institutional review board approval, we performed a retrospective review using the electronic medical record and administrative databases from Kaiser Permanente Southern California to identify all the patients there who were diagnosed with Dupuytren disease (contracture of palmar fascia, International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] diagnosis code 728.6) between 2007 and 2014. Any physician who evaluated the patient and determined the patient to have Dupuytren disease could make the diagnosis. All patients aged 18 years and older were included in the study. Patients without a BMI measurement within 1 year of diagnosis were excluded. Basic demographic data including age, sex, and ethnicity were collected. Body mass index, diabetes mellitus diagnosis (ICD-9-CM 250.00-93), and HbA1C (if diagnosed with diabetes mellitus) values were obtained from administrative databases. All data were collected at the time of the first recording of Dupuytren disease in the medical record and included all encounter types (new

and follow-up). A patient was counted once and was associated with a single BMI obtained at the time of diagnosis. The comparison group consisted of all adult patients from the Kaiser Permanente Southern California health system (aged greater than 18 years) in 2010 with at least one height and weight measurement. If patients had more than one measurement, only one randomly selected measurement was used for analysis. A single year was selected for use as the comparison group to prevent individual data from being collected for multiple years. We were careful to ensure that patients in the comparison group were counted only once and associated with a single BMI obtained from that year. Furthermore, 2010 was used for the control group because it was the midpoint of the study period (2007 to 2014) and was thought to reflect the average patient population best during that period. We divided BMI into previously defined categories (normal, 18.5 to 24.9; overweight, 25.0 to 29.9; obese class I, 30.0 to 34.9; obese class II, 35.0 to 39.9; and extreme obesity, 40+).¹³

Patient characteristics were compared between those who had and did not have Dupuytren disease using *t* test for continuous variables and chi-square test for categorical variables. Bivariate and multivariable logistic regression analyses were used to examine the association of Dupuytren disease with demographic data and BMI. After the bivariate regression analyses, clinically significant variables were added as a single block in the multivariate regression model. A second regression analysis of patients with diabetes and HbA1C values was performed with HbA1C levels, among other variables, in the regression model. Statistical significance was determined using P < .05.

RESULTS

Between 2007 and 2014, 14,844 patients were identified as having Dupuytren disease. The comparison group included 2,049,803 patients and consisted of all patients over aged greater than 18 years in 2010, with recent height and weight measurements (Table 1). Mean age of all patients was 47.8 years (range, 18–99 years; P < .05). Mean age of patients diagnosed with Dupuytren disease was 63.8; 90.7% were aged greater than 50 years (P < .05). Men made up 42.7% of the study population but comprised 58.8% of patients diagnosed with Dupuytren disease (P < .05). Caucasians made up 38.7% of the study population comparison group but made up 75.4% of patients with Dupuytren disease (P < .05).

There was a total of 2,791,437 adult enrollees (aged 18 years and older) in the health care plan and

TABLE 1. Patient Char	TABLE 1. Patient Characteristics, by Dupuytren Disease			
Demographic Information	Total $(N = 2,049,803)$	Negative for Dupuytren Disease ($N = 2,034,959$)	Positive for Dupuytren Disease ($N = 14,844$)	P Value
Age, y				< .05
Mean (SD)	47.8 (17.44)	47.7 (17.42)	63.8 (11.31)	
Median (range)	48.0 (18.0-99.0)	48 (18.0-99.0)	64 (18.0-99.00)	
Age, y (n [%])				< .05
18-39	713,939 (34.8)	713,559 (35.1)	380 (2.6)	
40-49	386,492 (18.9)	385,496 (18.9)	996 (6.7)	
50-59	404,511 (19.7)	400,959 (19.7)	3,552 (23.9)	
60-69	298,508 (14.6)	293,098 (14.4)	5,410 (36.4)	
≥ 70	246,353 (12)	241,847 (11.9)	4,506 (30.4)	
Sex (n [%])				< .05
Female	1,174,284 (57.3)	1,168,164 (57.4)	6,120 (41.2)	
Male	875,519 (42.7)	866,795 (42.6)	8,724 (58.8)	
Race/ethnicity (n [%])				< .05
Asian/Pacific Islander	201,091 (9.8)	200,736 (9.9)	355 (2.4)	
Black	202,930 (9.9)	202,388 (9.9)	542 (3.7)	
Hispanic	690,035 (33.7)	687,844 (33.8)	2,191 (14.8)	
Native American	4,473 (0.2)	4,440 (0.2)	33 (0.2)	
Other/multiple	32,587 (1.6)	32,485 (1.6)	102 (0.7)	
Unknown	126,052 (6.1)	125,624 (6.2)	428 (2.9)	
White	792,635 (38.7)	781,442 (38.4)	11,193 (75.4)	
BMI category (n [%])				< .05
<18.5	27,722 (1.4)	27,553 (1.4)	169 (1.1)	
18.5-24.0	589,256 (28.7)	584,951 (28.7)	4,305 (29)	
24.1-29.9	709,296 (34.6)	703,184 (34.6)	6,112 (41.2)	
30-34.9	423,040 (20.6)	420,184 (20.6)	2,856 (19.2)	
35-39.9	182,247 (8.9)	181,286 (8.9)	961 (6.5)	
≥40	118,242 (5.8)	117,801 (5.8)	441 (3)	

7,546 were diagnosed with Dupuytren disease before December 31, 2007. The prevalence of Dupuytren disease was 270 per 100,000 (0.3%). During the period between 2008 and 2014, 9,897 patients were newly diagnosed with Dupuytren disease among the 2,498,631 patients who remained from the original total before 2008 (2,791,437 patients). The incidence of Dupuytren disease was 79 cases per 100,000 person-years.

In the multivariate logistic regression analysis with age, sex, race/ethnicity, and BMI in the model, there was a significantly increased odds of Dupuytren disease diagnosis for ages 60 to 69 years (odds ratio [OR], 28.1; 95% confidence interval [CI], 25.3–31.2) and 70 years and older (OR, 25.1; 95% CI, 22.6–27.9) compared with ages 18 to 39 years (P < .05) (Table 2). All ethnicities had lower odds of Dupuytren disease compared with Caucasian patients

(P < .05). The risk of developing Dupuytren disease decreased with increasing BMI. The likelihood of Dupuytren disease was lowest in patients with extreme obesity (OR, 0.53; 95% CI, 0.48–0.58; P < .05).

In different regression analyses, when age or BMI was treated as a continuous variable, each additional year in age increased the odds of Dupuytren disease diagnosis by 4.7% (P < .05). An increase of 1 unit of BMI was found to decrease the odds of a diagnosis of Dupuytren disease by 3% (P < .05) (data not shown).

Among the study population of 2,049,803 patients, there was a total of 238,259 patients who had a diagnosis of diabetes mellitus (ICD-9-CM 250) and who had obtained an HbA1C level during the study period. Of this group, 3,418 patients (1.43%) also had a diagnosis of Dupuytren disease (Table 3).

TABLE 2. Adjusted	l ORs of Dupuytren	Diagnosis
Demographic Information	Adjusted OR (95% CI)	P Value

Age, y		
18-39	1.00 (reference)	
40-49	4.78 (4.25-5.38)	< .05
50-59	14.78 (13.28-16.43)	< .05
60-69	28.07 (25.28-31.18)	< .05
70+	25.07 (22.55-27.86)	< .05
Sex		
Female	1.00 (reference)	
Male	1.73 (1.68-1.79)	< .05
Race/ethnicity		
White	1.00 (reference)	
Asian/Pacific	0.14 (0.13-0.16)	< .05
Islander		
Black	0.24 (0.22-0.26)	< .05
Hispanic	0.37 (0.35-0.39)	< .05
Native American	0.67 (0.47-0.49)	< .05
Other/multiple	0.40 (0.33-0.49)	< .05
Unknown	0.46 (0.42-0.51)	< .05
BMI		
<18.5	0.88 (0.75-1.02)	.093
18.5-24.9	1.00 (reference)	
25.0-29.9	0.93 (0.90-0.97)	< .05
30.0-34.9	0.75 (0.71-0.79)	< .05
≥ 40	0.53 (0.48-0.58)	< .05

Caucasian men with diabetes were significantly more likely to be diagnosed with Dupuytren disease (62.8%; P < .05). A diagnosis of Dupuytren disease was associated with advanced age and lower BMI. Bivariate analysis revealed no significant difference in HbA1C values in patients with and without a diagnosis of Dupuytren disease; mean and median values of 7.5 and 7.1 were found in both groups.

We performed a multivariable logistic regression analysis to assess the relationship between Dupuytren disease and HbA1C level (Table 4). Using an HbA1C of less than 7.0 as the reference, HbA1C levels were categorized as 7.0 to 7.9, 8.0 to 8.9, and 9.0 to 9.9, and tested using a multivariable model. Adjusted OR of having a diagnosis of Dupuytren disease increased with increasing HgA1C (7.0 to 7.9, OR 1.19; 8.0 to 8.9, OR 1.32; and 9.0 to 9.9, OR 1.46). When HbA1C was greater than 10.0, the OR was still positively correlated with Dupuytren disease but the value dropped to 1.36 (P < .05). A 1-unit level increase of HbA1C (eg, increase from 7.0 to 8.0) had an adjusted OR of 1.08 for Dupuytren diagnosis (P < .05).

DISCUSSION

Dupuytren disease is largely seen in middle-aged white men, with a variable rate of progression among patients. Predicting which population of patients is at greatest risk of development of the disease, and of those patients who have it, which will progress to a contracture, is elusive. Investigating the relationship between obesity and Dupuytren disease could improve the counseling of patients, guide protective measures, and spur the development of new treatment modalities.

In this study, the calculated annual incidence of approximately 8 cases per 10,000 adults and the prevalence of 0.3% were similar to recently published annual incidence and prevalence data in the US population of 3 cases per 10,000 adults and 1%, respectively.¹⁴ The demographic pattern in the current population was also consistent with prior studies.^{3–8,15,16} We found an increased risk of Dupuytren diagnosis in older white male patients and discovered that the risk of Dupuytren disease was inversely related to obesity.

These findings are consistent with results from Gudmundsson et al,⁸ who also found an association of lower rates of Dupuytren disease in patients with higher BMI. Their population had a mean BMI of 25 for patients with Dupuytren disease, compared to 26.1 in patients who did not have the disease. Body mass was also on average 5.4 kg less in patients with Dupuytren disease than in patients without the disease. A significant strength of this study was the size and heterogeneous nature of the population. The study population of Gudmundsson et al was homogeneous (white Scandinavian) and small (2,165 people). The current patient population was over 2 million and was racially diverse.¹²

Geoghegan et al⁴ studied diabetes as a risk factor for Dupuytren disease. They found that patients who were treated with either metformin or insulin were at significant risk for Dupuytren disease (OR, 3.56 with metformin; OR, 4.38 with insulin). The sample size of the study was relatively small (821 patients and 1,642 control subjects) and did not show a correlation between BMI and Dupuytren disease.

The current data showed a correlation among BMI, HgA1C, and the diagnosis of Dupuytren disease; however, the study design does not allow us to evaluate causation. Therefore, we cannot draw conclusions as to why this correlation exists. However,

TABLE 3. Patients With	Diabetes Diagnosis and H	bA1C		
Demographic Information	Negative for Dupuytren Disease ($N = 234,841$)	Positive for Dupuytren Disease ($N = 3,418$)	Total $(N = 238,259)$	P Value
Age, y				< .05
Mean (SD)	61.0 (13.32)	65.1 (10.51)	61.0 (13.29)	
Median	61	65	61	
Range	(18.0–99.0)	(24.0-94.0)	(18.0-99.0)	
Age group (n [%])				< .05
18-39	13,862 (5.9)	46 (1.3)	13,908 (5.8)	
40-49	30,791 (13.1)	183 (5.4)	30,974 (13)	
50-59	60,293 (25.7)	758 (22.2)	61,051 (25.6)	
60-69	66,421 (28.3)	1,277 (37.4)	67,698 (28.4)	
≥ 70	63,474 (27)	1,154 (33.8)	64,628 (27.1)	
Sex (n [%])				< .05
Female	113,572 (48.4)	1,427 (41.7)	114,999 (48.3)	
Male	121,269 (51.6)	1,991 (58.3)	123,260 (51.7)	
Race/ethnicity (n [%])				< .05
Asian/Pacific Islander	27,491 (11.7)	143 (4.2)	27,634 (11.6)	
Black	29,539 (12.6)	180 (5.3)	29,719 (12.5)	
Hispanic	85,798 (36.5)	861 (25.2)	86,659 (36.4)	
Native American	568 (0.2)	8 (0.2)	576 (0.2)	
Other/multiple	2,304 (1)	20 (0.6)	2,324 (1)	
Unknown	6,047 (2.6)	61 (1.8)	6,108 (2.6)	
White	83,094 (35.4)	2,145 (62.8)	85,239 (35.8)	
BMI Category (n [%])				< .05
<18.5	1,125 (0.5)	12 (0.4)	1,137 (0.5)	
18.5-24.9	33,850 (14.4)	541 (15.8)	34,391 (14.4)	
25.0-29.9	73,099 (31.1)	1,272 (37.2)	74,371 (31.2)	
30.0-34.9	63,551 (27.1)	930 (27.2)	64,481 (27.1)	
35.0-39.9	35,531 (15.1)	416 (12.2)	35,947 (15.1)	
≥40	27,685 (11.8)	247 (7.2)	27,932 (11.7)	
BMI				< .05
Mean (SD)	31.7 (7.05)	30.4 (5.94)	31.7 (7.04)	
Median	30.6	29.5	30.6	
Range	(11.4-103.8)	(10.6-64.4)	(10.6-103.8)	
HbA1C (n [%])	· · · · ·		· · · ·	.04
<7.0	106,324 (45.3)	1,528 (44.7)	107,852 (45.3)	
7.0-7.9	63,522 (27)	963 (28.2)	64,485 (27.1)	
8.0-8.9	29,292 (12.5)	445 (13)	29,737 (12.5)	
9.0-9.9	15,229 (6.5)	230 (6.7)	15,459 (6.5)	
≥ 10	20,474 (8.7)	252 (7.4)	20,726 (8.7)	
HbA1C value	.,,	()		.86
Mean (SD)	7.5 (1.60)	7.5 (1.51)	7.5 (1.60)	
Median	7.1	7.1	7.1	
Range	(3.1–19.4)	(4.2–17.1)	(3.1–19.4)	

CABLE 4. Logistic Regression Results for		
Dupuytren Disease With Diabetes Mellitus	and	
HbA1c (N = $238,259$)		

Adjusted OR (95% CI)	P Value
0.968 (0.962-0.973)	< .05
1.00 (reference)	
1.19 (1.10-1.29)	< .05
1.32 (1.18-1.47)	< .05
1.46 (1.27-1.68)	< .05
1.36 (1.19-1.57)	< .05
1.025 (1.022-1.027)	< .05
	(95% CI) 0.968 (0.962–0.973) 1.00 (reference) 1.19 (1.10–1.29) 1.32 (1.18–1.47) 1.46 (1.27–1.68) 1.36 (1.19–1.57)

the correlation between low BMI and increased prevalence of Dupuytren disease or, for that matter, a protective mechanism from obesity warrants further analysis. Furthermore, although many diabetic patients are obese, the current findings showed that the relationship among Dupuytren disease, obesity, and diabetes is complicated: The risk of Dupuytren disease diagnosis increased with poor blood glucose control but decreased with obesity.

In 1983, Rabinowitz et al¹⁷ showed that the lipid composition of palmar fat differs in Dupuytren tissue compared with non-Dupuytren tissue. A prospective study showed an association between raised serum lipid levels and the pathogenesis of Dupuytren disease.¹⁸ These findings argue for a relationship between lipids and Dupuytren disease. It is well-known that abnormalities in lipid metabolism are associated with increasing BMI with an estimated 60% to 70% of obese patients being dyslipidemic.¹⁹ It is possible that body fat percentage rather than BMI would be a more useful factor to evaluate.

Regarding the role of diabetes, the current data showed a clear association of increasing HgA1C and increasing odds of Dupuytren diagnosis. The exception to this is that the adjusted OR for HgA1c greater than 10.0 was slightly less than for HgA1c 9.0 to 9.9, 1.36, and 1.46, respectively. This may be because of the comparatively small number of patients with elevated HgA1C greater than 10.0 (Table 4).

It has been established that patients with elevated blood glucose levels also have elevated levels of oxygen free radicals.²⁰ Murrell et al²¹ hypothesized that "production of free radicals may be an important factor in the pathogenesis of Dupuytren's contracture." Arkkila et al²² showed that in patients with type 1 diabetes, age and duration of diabetes, not control of it, were factors most closely associated with the development of Dupuytren disease. However, in their study, control of diabetes was determined by the development of diabetes-associated complications. It remains possible that increased blood glucose levels produce greater free oxygen species that, in turn, are involved in the development and/or progression of Dupuytren tissue. The current data support this theory by showing increased odds of Dupuytren disease diagnosis with increased HbA1C levels.

There are several limitations of the current study. It was retrospective and relied on the coding of all physicians, including primary care providers, who may not have been familiar with the diagnosis. Moreover, because of the nature of the data, it was not known when patients first developed Dupuytren disease and what their BMI was in the very early stages of the disease. An assumption made in the study was that the BMI data obtained for both patients who were positive and negative for Dupuytren disease reflected their normal BMI. Also assumed was that BMI in this population study does not fluctuate significantly over time. For an individual or small study, this assumption could not be made reliably. However, we believe that individual patient fluctuations in BMI are sufficiently small and will not appreciably affect BMI trends in this very large population study. With regard to mechanical factors, several authors have investigated repetitive stress and microtrauma to patients' hands as a possible risk factor for the development of Dupuytren disease.²³⁻²⁶ A potential confounding factor tat was not controlled for in the current study was activity level. It is possible that patients with normal BMI tend to be more active in the use of their hands, sustaining a greater degree of microtrauma, and thus they may have been at greater risk of developing symptomatic contractures. Future prospective studies will need to include activity level, specifically as it pertains to hand use, and hand dominance in the data collection and analyses. Another shortcoming is that the number of patients with low BMI (less than 18.5) was too small in the current study, which resulted in its being underpowered to draw conclusions from this specific patient group. Finally, BMI does not reflect body fat precisely. Therefore, the study and control groups likely included patients with high BMI but low body fat content. Conversely, patients with relatively high body fat content but low BMI were also likely included in the patient groups.

Future work could investigate the relationship of body fat percentage versus BMI and also BMI when patients first developed Dupuytren disease. It would also be important to determine whether BMI or body fat percentage is related to severity and/or recurrence of disease.

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ERRATUM

In the article by Hacquebord et al in the March 2017 issue of *The Journal of Hand Surgery* ("The Risk of Dupuytren Surgery in Obese Individuals", Vol 42, No. 3, p. 149-155), the title should have been "The Risk of Dupuytren Diagnosis in Obese Individuals." The authors apologize for this oversight.