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Analysis of a National Database Investigating Development of Trigger Finger after Treatment of Dupuytren Disease

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Background: Dupuytren disease is associated with inflammation and myofibroblast overgrowth, as is stenosing tenosynovitis (trigger finger). Both are linked with fibroblast proliferation, but a potential associative link between the diseases is unknown. The purpose of this study was to evaluate the progression of trigger finger following treatment for Dupuytren contracture in a large database.

Methods: A commercial database encompassing 53 million patients was utilized from January 1, 2010 to March 31, 2020. The study cohort included patients diagnosed with either Dupuytren disease or trigger finger utilizing International Classification Codes 9 and 10. Terminology codes were used to identify common Dupuytren procedures, as well as trigger finger release. Logistic regression analysis was used to define independent risk factors for developing trigger finger.

Results: A total of 593,606 patients were diagnosed with trigger finger. Of these patients, 15,416 (2.6%) were diagnosed with trigger finger after diagnosis of Dupuytren disease, whereas 2603 (0.4%) patients were diagnosed with trigger finger after treatment of Dupuytren contracture. Independent risk factors for trigger finger included age 65 years or older (OR 1.00, $P < 0.05$), diabetes (OR 1.12, $P < 0.05$) and obesity (OR 1.20, $P < 0.005$). Patients who received collagenase clostridium histolyticum treatment (OR 0.34, $P < 0.005$) for Dupuytren contracture were significantly less likely to develop trigger finger.

Conclusions: Dupuytren contracture is associated with inflammation and subsequent trigger finger development at a higher rate than the background population frequency. Collagenase clostridium histolyticum injection may lead to a decreased risk of trigger finger requiring surgical intervention in patients with risk factors.
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INTRODUCTION

Disease sequelae, as related to either the primary diagnosis or a surgical treatment, can be difficult to identify based upon the postoperative timeline. However, this limitation can be bridged by using very large datasets to better identify variances. One such previously unlinked disease state may be Dupuytren disease and triggering of the flexor tendons.

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Dupuytren disease[1–5] pathophysiology is secondary to fibroblast infiltration that causes increased collagen production along the bundles of fascia in the glabrous hand and foot. These myofibrillar bundles then undergo contracture and fibrosis in the resultant cord, which contract or fibrose.[6,7] Similarly, stenosing tenosynovitis (also known as trigger finger) is due to thickening of the flexor sheath and tenosynovium, with nodule formation along the flexor tendon, or a combination of both.[8,9] Despite the pathophysiology of these diseases sharing similar connective tissue pathways, there have been very few articles exploring the association between Dupuytren disease and trigger finger. Although prior authors have suggested that trigger finger symptoms may progress after a diagnosis of Dupuytren contracture, no population-based studies have explored risk factors for the development of trigger finger after the treatment of Dupuytren contracture.[10]

Disclosure statements are at the end of this article, following the correspondence information.

The aim of this study was to evaluate Dupuytren disease treatment and the progression of trigger finger, utilizing a large national database to characterize risk factors with greater associated statistical sensitivity. Large, comprehensive data sets also have the potential to mitigate bias when compared with smaller, high-quality data samples while concurrently answering questions about stable associations and correlations even in the absence of casual evidence.[11,12] As such, we aimed to identify if common treatments of Dupuytren contracture had an impact on the subsequent development of trigger finger as a causative or associated effect.

Takeaways

Question: Is there a potential link between treatment of Dupuytren contracture and increased or decreased risk of developing trigger finger?

Findings: A large insurance database with International Classification and Current Procedural Terminology codes was retrospectively reviewed in patients with Dupuytren disease for the development of trigger finger. Risk factors for trigger finger included age 65 years or older, diabetes, and obesity. Men and patients who received collagenase clostridium histolyticum treatment were less likely to develop trigger finger.

Meaning: Collagenase clostridium histolyticum treatment of Dupuytren contracture in patients with risk factors (ie, diabetes, obesity) for the development of trigger finger may decrease their risk of developing subsequent trigger finger.

METHODS

PearlDiver (PearlDiver Inc, Colorado Springs, CO), a commercially available administrative claims database with a national cohort of private payers encompassing 53 million unique patients, was queried from January 2010 to April 2020. Data were tracked across all episodes of care for patients in which their insurance was utilized at the time of Dupuytren disease treatment and followed for a minimum of at least 1 year for the development of trigger finger. To ensure the validity of the study, we utilized the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines, and checklists were utilized in performing the study.[13]

Patient Cohorts

The study cohort included any patient diagnosed with either Dupuytren contracture or trigger finger, utilizing both International Classification Codes (ICD) 9 and 10 (palmar fascia fibromatosis, ICD-9: 728.6 and ICD-10: M72.0; trigger finger, ICD-9 727.03 and flexor tendon tenosynovitis ICD-10: M65.30:35). Subgroup cohorts were created containing patients (1) diagnosed with trigger finger after diagnosis of Dupuytren disease and (2) diagnosed with trigger finger after treatment of Dupuytren disease (Fig. 1). Patients with less than 1 year of longitudinal follow-up were excluded.

Patient demographics included age and gender. Comorbid conditions include diabetes mellitus, hypothyroidism, rheumatoid arthritis, and obesity. The average Charlson Comorbidity Index (CCI) was recorded for all patients. The CCI is a validated, weighted index to measure burden of disease. Patients with a higher CCI have more comorbidities, higher disease burden, and subsequent lower rates of survival.[14] Social history included alcohol abuse and tobacco use.

Coding

Current Procedural Terminology (CPT) codes were used to identify Dupuytren contracture treatment procedures including collagenase clostridium histolyticum (CCH) injection (CPT 20527, J0775), percutaneous needle aponeurotomy (PNA) (CPT 26040), open fasciectomy (CPT 26123, 26125, 26121), and open fasciotomy (CPT 26045).

The CPT code 26055 was used to identify patients who underwent trigger finger release. To assure that all included patients had a tendon sheath incision for a trigger digit and not for some other diagnosis; only those patients with CPT code 26055 associated with an ICD-9 or ICD-10 diagnosis of trigger finger were included.

Statistical Analysis

Descriptive statistics were computed, using means and standard deviations. Logistic regression analysis was used to define independent risk factors for the development of trigger finger after diagnosis of Dupuytren disease, as well as any associations with common Dupuytren contracture treatments and subsequent progression of trigger finger that required operative intervention. Statistical analysis was conducted in PearlDiver and an unadjusted alpha level of 0.05 for significance was used for all tests.

RESULTS

A total of 593,606 patients were diagnosed with trigger finger in the study time period, and of these patients, 15,416 (2.6%) were diagnosed with trigger finger after being diagnosed with Dupuytren disease, whereas 2603 (0.4%) patients were diagnosed with trigger finger after treatment for Dupuytren contracture (Fig. 1).

Logistic regression demonstrated tobacco use (OR 1.10, $P < 0.05$), diabetes mellitus (OR 1.12, $P < 0.05$), and obesity (OR 1.20, $P < 0.005$) as significant independent risk factors for developing trigger finger after being diagnosed with Dupuytren disease (Table 1). Male gender was protective for development of trigger finger after diagnosis of Dupuytren contracture (OR 0.563, $P < 0.005$). Patients who underwent fasciotomy (n = 2149, 7%) or fasciectomy (n = 19,066, 61%) for Dupuytren contracture were more likely to be diagnosed with trigger finger requiring surgical release with odds ratios of 2.43 ($P < 0.005$) and 2.69 ($P < 0.005$), respectively. Patients who received CCH treatment (OR 0.34, $P < 0.005$) for Dupuytren contracture or had a history of alcohol abuse (OR 0.64, $p \leq 0.005$) were less likely to develop trigger finger. Dupuytren

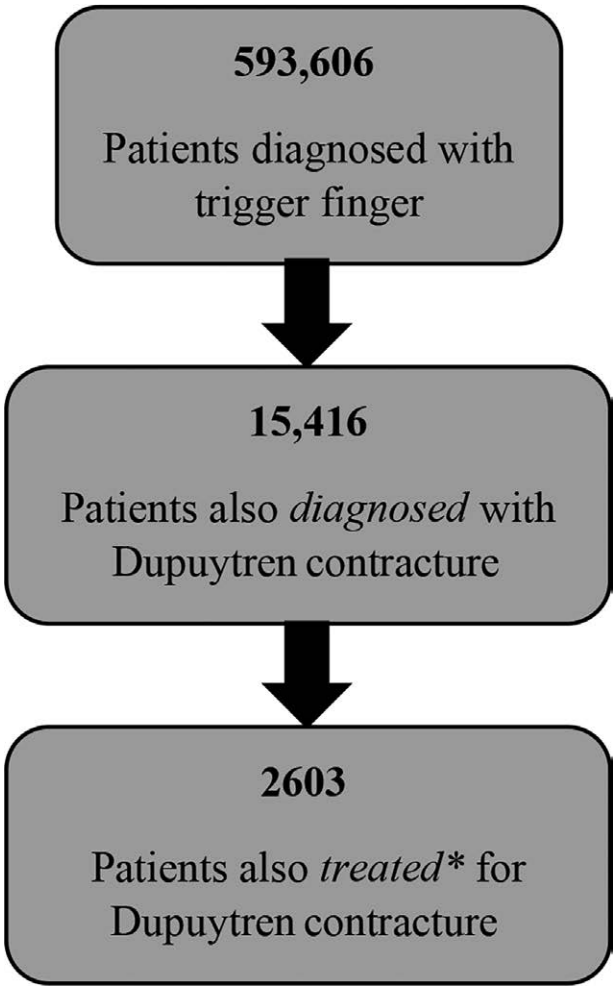

Fig. 1. Flow diagram illustrating breakdown of patient cohorts. *Treatment includes fasciotomy, fasciectomy, collagenase clostridium histolyticum injection, or PNA.

Table 1. Logistic Regression Analysis of Risk Factors for Diagnosis of Trigger Finger Requiring Operative Release after Diagnosis of Dupuytren Disease

Variable	Odds Ratio	Confidence Interval (95%)		*P*
Demographics				
Age, ≥65 y	**1.00388**	**1.00090**	**1.00689**	**<0.05**
Gender, men	**0.56361**	**0.53037**	**0.59887**	**<0.005**
Social history				
Alcohol abuse	**0.63660**	**0.55583**	**0.72577**	**<0.005**
Tobacco use	**1.10069**	**1.02825**	**1.17750**	**<0.05**
Comorbid conditions				
Diabetes	**1.11952**	**0.99920**	**1.25121**	**<0.05**
Hypothyroidism	1.02994	0.96570	1.09803	0.36782
Obesity	**1.19734**	**1.12342**	**1.27575**	**<0.005**
Rheumatoid arthritis	0.99951	0.87657	1.13495	0.99412
Procedure				
CCH	**0.33779**	**0.27012**	**0.41644**	**<0.005**
PNA	0.94023	0.77909	1.12422	0.50968
Fasciectomy	**2.43289**	**2.28063**	**2.59421**	**<0.005**
Fasciotomy	**2.69081**	**2.34195**	**3.07989**	**<0.005**

Bold text indicates a statistically significant finding.

Table 2. Number of Patients Receiving Most Common Procedures for Dupuytren Disease

Procedure	No. Patients (%)
CCH	6500 (21%)
PNA	3479 (11%)
Fasciectomy	19,066 (61%)
Fasciotomy	2149 (7%)

contracture treatment with PNA was not a statistically significant risk factor for the development of trigger finger. Hypothyroidism (OR 1.03, $P = 0.37$) and rheumatoid arthritis (OR 0.99, $P = 0.99$) were also not statistically significant risk factors for the development of trigger finger after Dupuytren disease diagnosis (Table 1). Of all treatment modalities, fasciectomy was the most common treatment for Dupuytren contracture with 19,066 patients (61%), followed by 6500 patients (21%) receiving CCH injections, 3479 patients (11%) undergoing PNA, and 2149 (7%) undergoing fasciotomy (Table 2).

Among the patients diagnosed with trigger finger after the diagnosis of Dupuytren disease (n = 15,416), 4959 (32.2%) underwent operative intervention for trigger finger with tendon sheath incision. Within this population, 2220 (45%) were men, 1256 (25%) were tobacco users, and 256 (5%) were diagnosed with alcohol abuse. Of the comorbid conditions analyzed, 2870 (58%) had diabetes mellitus, 1750 (35%) were obese, and 1584 (32%) had hypothyroidism (Table 3). The CCI score was 2.09 (median = 1, SD = 2.31).

DISCUSSION

This is the largest study to-date analyzing risk factors for development of trigger finger after Dupuytren contracture treatment. Following analysis among all patients with Dupuytren disease, 2.6% developed trigger finger after being diagnosed with Dupuytren disease, whereas 0.4% developed trigger finger after being treated for Dupuytren contracture. Fasciectomy and fasciotomy were associated with higher odds of subsequent trigger finger development, CCH was associated with lower odds of subsequent trigger finger development.

Flexor tendon stenosing tenosynovitis, or trigger finger, is very common, with a prevalence of 2% in the general population.[15,16] This study demonstrated an increased

Table 3. Demographic Data of Patients Diagnosed with Dupuytren Disease that Subsequently Required Surgical Release for Trigger Finger

	No. Patients (%)
Demographics	
Gender, men	2220 (45%)
Social history	
Alcohol abuse	246 (5%)
Tobacco use	1256 (25%)
Comorbid conditions	
Diabetes	2870 (58%)
Hypothyroidism	1584 (32%)
Obesity	1750 (35%)
Rheumatoid arthritis	266 (5%)

prevalence amongst patients with Dupuytren disease at 2.6%. The first report of Dupuytren contracture as cause of secondary trigger finger was made by Parker[17] in 1979, in which progression was noted in five patients. Burgess and Watson[18] reported a series of 47 patients who underwent excision of the A1 pulley and localized total fasciectomy for concurrent treatment of both diseases. In 2019, Yang et al[10] retrospectively analyzed a single surgeon cohort of 238 patients treated over 3 years for either Dupuytren contracture or trigger finger and found that Dupuytren disease was significantly associated with the development of trigger finger.

The current study also found a decreased risk of developing trigger finger after receiving CCH treatment for Dupuytren contracture, with an odds ratio of 0.34. Given that this odds ratio is very close to 0, it can be inferred that the CCH injection may have a strong association in limiting disease progression of trigger finger after treatment of Dupuytren contracture. This study also confirmed several known risk factors for trigger finger in the context of a preceding Dupuytren disease diagnosis. One risk factor was the relatively higher prevalence of trigger finger in older adults with metabolic diseases such as diabetes mellitus. Collagenase lyses collagen fibrils, notably types I and III, which are the most abundant types in fibrotic diseases like Dupuytren disease, but biopsied sites of fibroblasts from patients with Dupuytren contracture have demonstrated that CCH inhibits spreading, attachment and proliferation of fibroblasts in a dose and time dependent fashion.[19,20] Transcriptional analysis has also shown inhibition of various extracellular matrix components, cytokines and growth factors.[20] Thus, CCH may not only induce chemical fasciectomy, but it may also have effects on preventing trigger finger formation by downregulating extracellular matrix components, collagen formation, cytokines and growth factors.[20–22] Inhibition of this collagen matrix synthesis, through modalities like CCH, may attenuate the progression of trigger finger disease.

Unlike trigger finger, Dupuytren disease does not have a bimodal incidence and is most frequently diagnosed during the sixth decade of life.[2,3] Metabolic diseases such as diabetes mellitus are well known comorbid associations with both trigger finger and Dupuytren disease.[23–27] The estimated prevalence of trigger finger in the diabetic population ranges from 5% to 20%, compared with 1%–2% in the general population.[28,29] Although the complete etiology of diabetic trigger finger is unclear, hyperglycemia may result in increased collagen cross-linking while conferring a resistance to degradation, therefore causing collagen accumulation.[30] The pathologic basis of Dupuytren disease also involves abnormal collagen synthesis, in which myofibroblasts produce pathologic amounts of collagen, notably type III. Broekstra et al[23] reported that diabetic patients carry a 3.06 increased risk of developing Dupuytren disease as oxidative stress results in advanced-glycated end-products that attach to cell receptors and up-regulate cytokines like transforming growth (TGF)-β.[31] Therefore, it is likely that the same pathologic pathway of diabetes mellitus contributes in some part to the possible progression of trigger finger from Dupuytren disease.

Patients treated for Dupuytren contracture with fasciectomy or fasciotomy were more likely to develop trigger finger that required tendon sheath incision, with odds ratios of 2.4 and 2.7, respectively. This indicates that in patients undergoing fasciectomy or fasciotomy for Dupuytren contracture, the odds of developing trigger finger was 2.4 and 2.7 times greater than the odds of not having either of these procedures and subsequent development of trigger finger. Fasciectomy and fasciotomy may induce cellular cascades resulting in metaplastic changes in the flexor tendon and sheath either directly or indirectly during the postoperative wound healing process. This may induce patients predisposed to trigger finger formation to subsequently develop trigger finger after fasciectomy or fasciotomy. As proposed by Burgess and Watson[18] and Yang et al,[10] it is suspected that operating through the diseased facia in Dupuytren contracture increases fibrosis and collagen deposition, causing the palmar fascia to hypertrophy and thicken with contracture of the palm. Furthermore, fasciotomy and fasciectomy procedures have higher rates of recurrence compared with dermofasciectomies in which the skin over the nodule and perinodular fat is excised, suggesting that surrounding tissue may be involved in the fibroproliferative process of Dupuytren disease.[32,33]

Treatment of Dupuytren contracture with CCH may also avoid perioperative morbidities and decrease costs associated with trigger finger treatment in patients predisposed to this pathology.[34–37] Open surgical release of the A1 pulley has high rates of success with minimal morbidity and recurrence and is therefore considered the gold standard treatment.[30,38] Kerrigan et al[39] demonstrated that two steroid injections followed by surgery was the least costly treatment strategy for all patients, while controversy remains around the treatment algorithm of diabetic trigger finger.[39–41] Total cost of trigger finger care for patients adherent to this aforementioned algorithm averaged $503, compared with an average of $3481 for patients who were not adherent to the algorithm.

Male gender was protective for development of trigger finger after diagnosis of Dupuytren disease. It is well established that men are more likely to have Dupuytren disease, with some published ratios as high as nine to one, but women are more likely to have trigger finger.[5,42] However, the pathologic basis behind how gender acts as in increased/decreased risk factor for either disease is not well known. Male gender may serve as a decreased risk factor for trigger finger due to lower levels of circulating estrogen levels. Trigger finger and de Quervain's tenosynovitis demonstrate similar pathologic changes with fibrosed thickening of the fibrous tendon sheath and fibrocartilaginous metaplasia, and an analysis of de novo estrogen receptor expression in stenosing tenosynovitis of the first dorsal wrist compartment (ie, de Quervain disease) demonstrated direct correlation with disease severity.[43] Shen et al demonstrated that estrogen receptor expression began with disease onset and peaked with disease severity, which was associated with tissue inflammation and angiogenesis.[43]

As with all studies that utilize large insurance databases, this study has several limitations.[16,44,45] Power of analysis is

dependent on the accuracy and quality of the coded data which may be prone to errors. This may skew the risk factor outcomes as well as timepoints between diagnoses and procedures. However, this study did not explore at which time trigger finger developed after treatment of Dupuytren contracture. Additionally, these data are only representative of patients in the United States with private insurance, which may not be generalizable to other populations (ie, uninsured patients). Furthermore, diagnostic codes before the 10th revision of the International Statistical Classification of Disease and Related Health Problems (ICD-10) did not differentiate Dupuytren disease from contracture, so unfortunately, data from these patients are mingled. However, patients with Dupuytren disease severe enough to develop contracture were specifically analyzed, as only this cohort would likely undergo invasive interventions (ie, PNA, CCH, fasciectomy, fasciotomy). The authors chose to include the ICD-9 codes with ICD-10 codes to maximize sample size to increase statistical power. It is well established that both Dupuytren disease and trigger finger have known genetic predispositions and are not sporadic diseases.[46–48] Therefore, given that the development of either disease is multifactorial with several systemic predisposing risk factors, it is reasonable to not limit analysis to same handedness.

CONCLUSIONS

Large data sets are well equipped to longitudinally identify disease patterns, risk factors and associations while allowing for inferences on subgroup patient populations.[49,50] There may be an association between Dupuytren contracture and trigger finger disease, both in shared pathways of inflammatory physiology and potential precipitating or causative effects.

Tobacco use, diabetes mellitus, and obesity may be risk factors in patients with Dupuytren contracture for the subsequent development of trigger finger, as are fasciotomy and fasciectomy. Clostridium histolyticum injections and male gender may be protective for the development of trigger finger after Dupuytren contracture treatment. Clostridium histolyticum injections for treatment of Dupuytren contracture in patients who have risk factors (ie, tobacco use, diabetes, obesity) for the development of trigger finger may decrease their risk of developing subsequent trigger finger.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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