

Research Articles

Opioid Use Is Associated with Increased Risk of Sepsis and Joint Stiffness in Patients with Pyogenic Flexor Tenosynovitis

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Objectives

The purpose of this study was to evaluate outcomes of patients with pyogenic flexor tenosynovitis with a history of opioid use disorder.

Methods

This study utilized the TriNetX database to identify patients aged > 18 years with a history of pyogenic flexor tenosynovitis by CPT code 26020 between January 1, 2015, and January 1, 2025. Concurrent diagnosis of OUD differentiated the experimental group from the control, which could not account for the route of administration. Next, one-to-one propensity matching was performed to balance the groups based on demographic characteristics and comorbidities, returning 734 matched pairs. Outcomes were assessed at one month following the incidence of PFT using relative risk (RR) and 95% confidence intervals (CI). P-value < 0.05 reflects statistical significance.

Results

Patients with PFT and a history of opioid use disorder were at increased risk of sepsis (RR 2.22, 95% CI (1.286, 3.839)) and joint stiffness (RR incalculable due to no instances of outcome in the control group). There were no differences in amputation rate, repeat irrigation and debridement, contracture, or osteomyelitis.

Conclusion

Pyogenic flexor tenosynovitis is associated with increased risk of sepsis and joint stiffness in patients with opioid use disorder. Given the higher risk of sepsis, patients with a history of OUD presenting with PFT should follow the respective hospital's sepsis algorithm and protocol. Likewise, early initiation of hand therapy may be considered to reduce the risk of permanent stiffness.

INTRODUCTION

Pyogenic flexor tenosynovitis (PFT) is an acute, rapidly progressive bacterial infection of the flexor tendon sheath of the hand, most often resulting from penetrating trauma such as a puncture wound or laceration to the finger.¹ The most common causative organisms are *Staphylococcus aureus* and *Streptococci* species, though other pathogens may be involved, especially with specific exposures.² This condition can affect all age groups, but is most frequently seen

in healthy adults and those with occupational or recreational hand injuries. The risk is further increased in individuals with diabetes or the immunocompromised, and has been on the rise amongst individuals who use intravenous drugs.^{2,3} PFT represents between 2.5% and 9.5% of all hand infections, and confers significant morbidity, particularly when treatment is delayed.^{1,2} Bacteria enter the flexor tendon sheath via direct penetrating trauma and can rapidly multiply using the synovial fluid as a medium. Infection may rapidly progress unimpeded along the entire

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length of the flexor tendon compartment, eventually compressing adjacent neurovascular structures and compromising the integrity of the flexor tendon itself.⁴ In some instances, when the index inoculation occurs in either the first or fifth digit, infection may spread via bursal communication to the opposite side of the hand, resulting in a “horseshoe” abscess.^{5,6}

Despite the identification of certain radiographic parameters that may differentiate PFT from other non-PFT hand infections, pyogenic flexor tenosynovitis remains a clinical diagnosis, and a thorough physical examination is crucial.^{6,7} First described by Kanavel in 1912, the four signs that bear his namesake are extensively used in the clinical setting to diagnose PFT and are described as follows: “1. Exquisite tenderness of the course of the sheath, limited to the sheath. 2. Flexion of the finger. 3. Exquisite pain on extending the finger, most marked at the proximal end;” the fourth sign, absent from Kanavel’s origin manuscript is “the whole of the involved finger is uniformly swollen.”^{8,9} These four cardinal signs have been examined extensively in the current literature, and although they demonstrate high sensitivity for the detection of PFT, the specificity of the four individual signs is relatively low.¹⁰ Thus, in addition to physical examination, there should be considerable emphasis placed on the patient’s history to achieve high diagnostic accuracy of this infection, particularly when one or more signs are absent.

While a few individual risk factors for the development of pyogenic flexor tenosynovitis have been identified, intravenous (IV) drug use has been associated with the incidence of septic tenosynovitis of the extremities. Reinus, Cotiis, and Schaffer 2015 described 20 individual cases of extensor tenosynovitis in which all patients had a known history of IV drug use.¹¹ This description parallels a previous case series by Dhaliwal and Garnes 1982 in which five instances of extensor tenosynovitis were reported following inadvertent injection of drugs into the extensor sheath of the hand.¹² Although opioid use has been identified as a risk factor for the disease, to the authors’ knowledge, there has been no study examining the outcomes of pyogenic flexor tenosynovitis in patients with a history of opioid use. Thus, our goal is to conduct a retrospective cohort study utilizing the TriNetX database to investigate outcomes of pyogenic flexor tenosynovitis in patients with a history of opioid drug use.

METHODS

The study utilized the TriNetX Research Network database (Cambridge, Massachusetts), a global healthcare data network that compiles de-identified, electronic medical data from over 120 healthcare organizations (HCOs) encompassing over 250 million patient lives.¹³ Participating HCOs permit the use of their information in exchange for access to the platform’s research capabilities at no additional cost, which include clinical trial protocol design, database query, and drug safety analysis. The TriNetX network is compliant with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Security Rule and certified according to

the ISO 27001:2013 standard. For these reasons, the study conferred minimal risk to patient privacy and was exempt from institutional review board approval and informed consent at our institution.

All data included in this analysis were obtained on June 13, 2025, from the TriNetX Research Network database within the ten years beginning January 1, 2015, and ending January 1, 2025. Inclusion criteria, exclusion criteria, propensity score matching criteria, and study endpoints utilizing classifications outlined by the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes or Current Procedural Terminology (CPT) codes. Patient cohorts were first established by querying the TriNetX database for all patients aged 18 years and older who underwent drainage of the tendon sheath, digit, and/or palm (CPT 26020) within the study period. It was determined that use of this code was most appropriate as multiple different ICD-10 codes can be used to describe pyogenic flexor tenosynovitis, and the TriNetX platform, by its nature, offers no way to access individual patient charts for cross-reference. Patients were then separated into experimental and control groups with the inclusion or exclusion criteria, respectively, of a history of opioid use (ICD-10 F11). This initial query yielded 740 patients in the opioid exposed group and 5,681 patients in the control group.

Next, the two cohorts were prepared for 1:1 propensity matching to limit the potential for confounding covariates. The characteristics chosen for matching included age at index, sex, race, and ethnicity, as well as a variety of medical comorbidities, some of which are associated with poor prognosis of infectious tenosynovitis.¹⁴ Patients who lacked data for any of the matching criteria were excluded from the analysis. Successful cohort matching was reflected by a P-value less than or equal to 0.05. Propensity score matching yielded a total of 734 pairs, representing the final study population.

A variety of outcomes were chosen for comparison between the two cohorts at one month following index infection. Statistical analysis was automatically performed by the TriNetX platform utilizing risk, or the number of instances of the event within the cohort, relative risk (RR), and 95% confidence intervals (CI). In situations where one cohort did not have a single instance of the event, the relative risk could not be calculated. P-value < 0.05 was considered to be statistically significant.

RESULTS

Following propensity matching before analysis, the two cohorts were similar in every demographic characteristic and all medical comorbidities except for the presence of vascular disease [Table 1].

Comparison of the two cohorts revealed that patients with a history of opioid use were more likely to develop sepsis following the incidence of pyogenic flexor tenosynovitis (RR = 2.222, 95% CI [1.286, 3.839]). Opioid use was also associated with significantly higher rates of ankylosis, defined as joint stiffness, at one month, although no instances of stiffness were present in the control group [Table 2].

Table 1. Baseline Demographic Information and Propensity Matching.

	Before Matching				After Matching			
Demographic	OUD (+)	OUD (-)	P-value	Std Diff.	OUD (+)	OUD (-)	P-value	Std Diff.
Age at Index	42.2 (12.3)	48.5 (16.7)	<0.001	0.432	42.2 (12.3)	41.1 (14.0)	0.124	0.080
Male	431 (58.2)	3585 (63.1)	0.010	0.100	429 (58.4)	438 (59.7)	0.633	0.025
Female	309 (41.8)	2096 (36.9)	0.010	0.100	305 (41.6)	296 (40.3)	0.633	0.025
White	601 (81.2)	4022 (70.8)	<0.001	0.246	595 (81.1)	614 (83.7)	0.193	0.068
Black or African American	83 (11.2)	916 (16.1)	0.001	0.143	83 (11.3)	81 (11.0)	0.868	0.009
Asian	10 (1.4)	150 (2.6)	0.034	0.092	10 (1.4)	10 (1.4)	1	<0.001
American Indian or Alaska Native	10 (1.4)	49 (0.9)	0.190	0.047	10 (1.4)	10 (1.4)	1	<0.001
Other Race	32 (4.3)	243 (4.3)	0.953	0.002	32 (4.4)	24 (3.3)	0.276	0.057
Hispanic or Latino	34667 (8.3%)	1063894 (6.9%)	0.233	0.048	74 (10.1)	53 (7.2)	0.051	0.102
Not Hispanic or Latino	577 (78.0)	4219 (74.3)	0.029	0.087	572 (77.9)	588 (80.1)	0.305	0.054
Comorbidities								
Diabetes Mellitus	136 (18.4)	1351 (23.8)	0.001	0.133	134 (18.3)	118 (16.1)	0.268	0.058
Vascular Disease	105 (14.2)	608 (10.7)	0.005	0.106	104 (14.2)	65 (8.9)	0.001	0.167
Obesity	128 (17.3)	1043 (18.4)	0.482	0.028	126 (17.2)	114 (15.5)	0.397	0.044
Chronic Kidney Disease	71 (9.6)	584 (10.3)	0.562	0.023	68 (9.3)	49 (6.7)	0.067	0.096
HIV	29 (3.9)	59 (1.0)	<0.001	0.186	26 (3.5)	25 (3.4)	0.887	0.007
Rheumatoid Arthritis	33 (4.5)	154 (2.7)	0.008	0.094	31 (4.2)	16 (2.2)	0.026	0.116
Lupus	10 (1.4)	23 (0.4)	0.001	0.102	10 (1.4)	10 (1.4)	1	<0.001
Gout	27 (3.6)	231 (4.1)	0.586	0.022	25 (3.4)	15 (2.0)	0.109	0.084
Hepatitis	25 (3.4)	64 (1.1)	<0.001	0.152	21 (2.9)	21 (2.9)	1	<0.001

Legend - continuous variables reported as mean ($\pm$ standard deviation), categorical variables as n (% of cohort). Abbreviations - HIV, human immunodeficiency virus; OUD (+), history of opioid use; OUD (-), no history of opioid use; Std. Diff., standard difference.

There was no difference in rates of digit amputation, although patients in the opioid exposure group had a higher absolute rate of amputation at one month. Additionally, there were no differences in osteomyelitis, contracture, digital nerve injury, or repeat irrigation and debridement at the study cutoff. Lastly, there were no instances of flexor tendon rupture or flexor tendon repair in either of the two study cohorts [Table 2].

DISCUSSION

This retrospective analysis found that opioid use disorder (OUD) was associated with a significantly higher incidence of sepsis and joint stiffness following the incidence of pyogenic flexor tenosynovitis (PFT). While prior research has identified intravenous (IV) drug use as a risk factor for PFT, this is, to the authors' knowledge, the first study to demonstrate a statistically significant association between PFT, sepsis, joint stiffness, and OUD regardless of the route of administration.¹¹ Utilizing ICD-10 codes to identify both PFT and OUD, this study investigates the opioid-related

Table 2. One Month Outcomes Following Incidence of Pyogenic Flexor Tenosynovitis.

	Risk in OUD (+)	Risk in OUD (-)	Risk difference	Relative Risk (95% CI)	P-value
Amputation	0.042	0.030	0.012	1.409 (0.824, 2.410)	0.208
Sepsis	0.054	0.025	0.029	2.222 (1.286, 3.839)	0.003
Flexor Tendon Rupture	0.000	0.000	0.000	0.000	0.000
Osteomyelitis	0.014	0.014	0.000	1.000	1.000
Contracture	0.014	0.014	0.000	1.000	1.000
Ankylosis	0.014	0.000	0.014	n/a	0.002
Aseptic Necrosis	0.000	0.014	-0.014	n/a	0.002
Flexor Tendon Repair	0.000	0.000	0.000	0.000	0.000
Digital Nerve Injury	0.014	0.014	0.000	1.000	1.000
Repeat I&D	0.050	0.069	-0.019	0.725	0.124

Legend - risk is the proportion of the cohort with the disease. Abbreviations - Repeat I&D, subsequent irrigation and debridement; OUD (+), history of opioid use; OUD (-), no history of opioid use.

risk for sepsis beyond direct inoculation from IV drug use or skin-penetrating trauma. By propensity matching the cohorts, researchers were able to limit the effects of confounding variables such as diabetes, peripheral vascular disease, and immunocompromised states, all of which are correlated to an increased risk of both pyogenic flexor tenosynovitis and sepsis.¹⁴ These findings align with an expanding body of literature that implicates OUD as a major risk factor for deep tissue and musculoskeletal infections, particularly of the hand and upper extremity.

Although IV drug use is a well-established contributor to hand infections through direct pathogen inoculation and penetrating trauma, the elevated risk observed amongst patients with OUD that cannot account for the route of administration suggests that other mechanisms, such as opioid-induced immunosuppression and behavioral risk factors, also play a role in susceptibility to infection and progression to sepsis.^{15,16} Opioids that metabolize to morphine, including oral codeine and intravenous heroin, have demonstrated immunosuppressive effects on both innate and adaptive immune responses.^{17,18} When administered orally, opioids can exert systemic immunosuppressive effects even in the absence of a primary infection, highlighting the relevance of non-injection routes in the pathogenesis of infection.¹⁹ These results are consistent with prior large-scale retrospective cohort data showing increased rates of deep tissue infections in patients with OUD receiving oral opioid agonist therapy.²⁰ While PFT may represent a confounding variable given the established relationship between opioid use and incidence of sepsis, we believe that the outcome time point is sufficiently narrow to hypothesize that PFT and incidence of sepsis are related.²¹ Regardless, the incidence of sepsis in the control group may indicate that PFT is not a purely isolated infection that could plausibly result in hematogenous spread, leading to bacteremia and systemic infection.

The presence of joint stiffness one month following PFT diagnosis in patients with opioid use disorder has not been previously associated in the literature. Though no studies address the direct effect opioids have on joint stiffness, the aforementioned immunosuppressive properties of opioids

have been linked to higher rates of septic arthritis and prosthetic joint infection, providing a possible explanation.^{22,23} Additionally, it is important to note that the diagnosis code for joint stiffness chosen for this analysis does not specify which joint is involved, so the exact location remains unclear.

The clinical implications of these findings are substantial. PFT is a surgical emergency with high morbidity, and delays in diagnosis or treatment can lead to devastating outcomes. Given that individuals with OUD often experience barriers to care and are more likely to leave against medical advice, they face elevated risks for poor functional outcomes, including digit loss or amputation.²⁴ These data highlight a concerning intersection of healthcare inequity, substance use disorder, and surgical urgency, and suggest that patients with OUD should be considered a high-risk group for PFT. Given the higher risk of sepsis, patients with a history of opioid use disorder presenting with PFT should follow the respective hospital's sepsis algorithm and protocol. Likewise, early initiation of hand therapy may be considered to reduce the risk of permanent stiffness. Particularly with this patient population, we recommend collaboration between the treating provider and social work services to address potential barriers to starting hand therapy, such as food insecurity or financial constraint.

This study has several inherent limitations. First, due to its retrospective nature, it is subject to selection bias as the study sample may not accurately represent the entire population. Additionally, the TriNetX research platform does not permit access to individual patient charts, so there is no way to verify diagnosis and procedure codes with provider documentation secondarily.²⁵ There is also a risk of improper coding, meaning that the study sample may underestimate or overestimate the true prevalence of PFT. As a result, future efforts should be directed towards prospective studies that can more accurately estimate the true risk profile of pyogenic flexor tenosynovitis in patients with opioid use disorder.

CONCLUSION

In summary, patients with pyogenic flexor tenosynovitis (PFT) and a history of opioid use disorder (OUD) are at increased risk of sepsis and joint stiffness. These findings underscore the importance of medical history taking in the workup of PFT in conjunction with thorough physical examination.

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DECLARATION OF CONFLICT OF INTEREST

The authors do NOT have any potential conflicts of interest for this manuscript

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DECLARATION OF ETHICAL APPROVAL FOR STUDY

Ethical approval was not required for this study as it utilized a HIPAA-compliant database without identifiable patient information.

DECLARATION OF INFORMED CONSENT

There is no information in the submitted manuscript that can be used to identify patients.

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