

Philadelphia College of Osteopathic Medicine

DigitalCommons@PCOM

---

PCOM Physician Assistant Studies Student  
Scholarship

Student Dissertations, Theses and Papers

---

2021

## Does Collagenase Injection Decrease Recurrence Rates Greater than Percutaneous Needle Fasciotomy in the Treatment of Dupuytren's Contracture?

Elisabeth Cawley

*Philadelphia College of Osteopathic Medicine*

Follow this and additional works at: [https://digitalcommons.pcom.edu/pa\\_systematic\\_reviews](https://digitalcommons.pcom.edu/pa_systematic_reviews)



Part of the [Medicine and Health Sciences Commons](#)

---

### Recommended Citation

Cawley, Elisabeth, "Does Collagenase Injection Decrease Recurrence Rates Greater than Percutaneous Needle Fasciotomy in the Treatment of Dupuytren's Contracture?" (2021). *PCOM Physician Assistant Studies Student Scholarship*. 583.

[https://digitalcommons.pcom.edu/pa\\_systematic\\_reviews/583](https://digitalcommons.pcom.edu/pa_systematic_reviews/583)

This Selective Evidence-Based Medicine Review is brought to you for free and open access by the Student Dissertations, Theses and Papers at DigitalCommons@PCOM. It has been accepted for inclusion in PCOM Physician Assistant Studies Student Scholarship by an authorized administrator of DigitalCommons@PCOM. For more information, please contact [library@pcom.edu](mailto:library@pcom.edu).

**Does Collagenase Injection Decrease Recurrence Rates Greater than Percutaneous Needle Fasciotomy in the Treatment of Dupuytren's Contracture?**

Elisabeth Cawley, PA-S

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies  
Philadelphia College of Osteopathic Medicine  
Suwanee, Georgia

December 15, 2020

## ABSTRACT

**Objective:** The objective of this selective EBM review is to determine whether or not collagenase injection decreases recurrence rates greater than percutaneous needle fasciotomy in the treatment of Dupuytren's contracture.

**Study Design:** A systematic review of three randomized control trials.

**Data Sources:** The reviewed articles were written in English and published in peer-reviewed journals between 2016 and 2017. These articles were chosen based on their ability to answer the proposed question of this review and obtained through Cochran and PubMed databases.

**Outcomes Measured:** Outcomes were measured by the recurrence of contractures, which is defined as passive extension deficits of 20-30 degrees post-treatment or requiring additional treatment after initial therapy.

**Results:** Scherman et al. (*J Hand Surg Eur Vol.* 2018;43(8):836-840. doi: 10.1177/1753193418786947.) concluded there was no statistically significant difference in 3-year recurrence rates between collagenase injection and needle fasciotomy (P-value >0.05). Stromberg et al. (*J Hand Surg A.* 2016;41(9):873-880. doi: 10.1016/j.jhsa.2016.06.014.) found similar 1-year recurrence rates in the treatment of MCP joint Dupuytren's contractures with collagenase injection and needle fasciotomy (P-value >0.05). Skov et al. (*J Hand Surg Am.* 2017; 42(5):321-328.e3. doi: S0363-5023(16)30817-6.) concluded collagenase injection and needle fasciotomy had similar 1-year recurrence rates in the treatment of PIP joint Dupuytren's contractures (P-value >0.05).

**Conclusions:** Based on the analysis of three randomized controlled trials, there is no significant difference in the rate of contracture recurrence between CCH injection and PNF at the 1 and 3-year follow-up mark. Variability among the treated joint and digit among the reviewed studies and non-blinding of evaluators may have impacted these results. Given the similarities in recurrence rates, it may be beneficial if future studies are directed toward other patient-oriented outcomes: associated healthcare cost, adverse events, visits required, and patient satisfaction.

**Keywords:** Dupuytren's contracture, recurrence rates, needle fasciotomy, collagenase injection.

## INTRODUCTION

Dupuytren's disease (DD) is a benign, slow-progressing, condition characterized by the formation of fibrous cords in the palmar fascia that causes flexion contractures of the digits. These contractures can impede normal hand function by causing deficits in the normal range of extension in single, or multiple digits. Often the joints of the hand are affected including the metacarpophalangeal (MCP), proximal interphalangeal (PIP), and the distal interphalangeal (DIP) joint. Given the gradual progression of this disease, the prevalence of DD increases with age. The overall prevalence of Dupuytren's disease in Western populations is 12% in those aged 55 and 29% in those aged 75 years old.<sup>1</sup> The annual incidence in the U.S. is approximately 3 cases per 10,000 adults.<sup>2</sup> DD is the most common hereditary connective tissue disorder and has a higher pervasiveness in patients with comorbidities such as hypertension, diabetes, ischemic heart disease, COPD, hyperlipidemia, and rheumatoid arthritis.<sup>3</sup> In addition to the known strong genetic predisposition of DD, there are environmental risk factors, such as smoking, alcohol use, and previous hand injuries. As the number of those afflicted by such diseases within the United States continues to rise, so does the necessity for providers to be knowledgeable in the aspects of Dupuytren's disease and its treatment. Physician Assistants may evaluate a Dupuytren's patient upon initial presentation and contribute throughout their care, rendering this common disease pertinent to the practicing PA.

In the matter of cost, an exact number for the total healthcare cost of DD has not been identified. However, in 2019 the cost of treatment for a single finger contracture ranges from \$7,657-8,519.<sup>2</sup> It has also been shown that those with DD utilize more medical services such as physical therapy, ED visits, outpatient surgery, etc.<sup>4</sup> There is not a precise estimate available

regarding how many healthcare visits are DD related; however, in 2014, 3 million Dupuytren's patients suffered a contracture severe enough to warrant a procedure.<sup>1</sup>

The etiology of DD is unknown; however, it involves fibroblastic and collagen deposition in the palmar fascia which produces cord-like structures. The 4<sup>th</sup> and 5<sup>th</sup> digit is commonly affected first, sparing the index finger and thumb. Men typically exhibit symptoms earlier than women and may include the development of a painless nodule of the palm, dimpling, or puckering of the skin. Loss of active and passive extension sequentially develops over time producing an abnormal curvature of the fingers and the inability to fully straighten the hand. Depending on the severity of the contracture, a patient's quality of life and the ability to perform daily tasks can be greatly impacted. There is no known cure for DD and the recurrence of these hand contractures frequently occurs.

The modalities used to treat Dupuytren's disease include physical therapy, glucocorticoid injection, collagenase *Clostridium histolyticum* (CCH) injection, percutaneous needle fasciotomy (PNF), and open fasciotomy. These treatments all play a role at certain stages of the disease, however, once an extension deficit reaches 20 degrees or more, a procedure is typically warranted to correct the contracture.

In 2009, CCH became the newest, non-surgical treatment aimed at enzymatically disrupting the palmar cords to release the contracture.<sup>5</sup> The procedure involves injecting CCH into a palpable cord, followed by passive extension manipulation one day later to disrupt the cord. Prior to the introduction of CCH, percutaneous needle fasciotomy was the widely accepted inexpensive, minimally invasive technique for contracture release. Being minimally invasive, both CCH and PNF are treatment options that have the benefit of causing less tissue damage than open fasciotomy, yet overall are considered less effective in comparison.

## **OBJECTIVE**

The objective of this selective EBM review is to determine whether or not collagenase injection decreases recurrence rates greater than percutaneous needle fasciotomy in the treatment of Dupuytren's contracture.

## **METHODS**

Studies compared in this review include three randomized controlled clinical trials that analyzed the efficacy of CCH injection against PNF in the treatment of Dupuytren's contractures. The population being studied included adult patients with a single Dupuytren's contracture who received the intervention of either CCH or needle fasciotomy. Patient outcomes included one, and three-year recurrence rates of contractures.

Keywords used to search for these studies included "Dupuytren's contracture", "needle fasciotomy", "collagenase injection" and were found via Cochran and PubMed databases. These peer-reviewed articles were selected by their relevance to the proposed topic, the inclusion of patient-oriented outcomes, and fulfillment of inclusion criteria. All three articles were published in English. Inclusion criteria consisted of studies that were randomized control trials, written in English, and conducted in adult patients. Exclusion criteria included studies published before 2010, pediatric patients, and secondary research. Additional inclusion and exclusion criteria may be found in Table 1. Statistics reported and utilized in this EBM review include relative risk reduction (RRR), absolute benefit increase (ABI), numbers needed to treat (NNT), and p-values.

## **OUTCOMES MEASURED**

The outcomes measured for this EBM review are the recurrence of a contracture post-treatment or needing an additional procedure after initial therapy. All three studies defined recurrence as a passive extension deficit (PED) that measured greater than 20-30 degrees or more

using a goniometer. Measurements were performed by either a nurse or physiotherapist at the 1 or 3-year follow up mark.<sup>5-7</sup>

**Table 1. Demographics & Characteristics of Included Studies**

Study	Type	# Pts	Age (years)	Inclusion	Exclusion	W/D	Interventions
Scherman (2016)	RCT	93	>18	Primary DD, palpable cord, total passive extension deficit between 30-135 degrees.	Previous treatment, thumb contractures, extension deficit less than 30 degrees.	2	CCH injection vs. Needle fasciotomy.
Stromberg (2016)	RCT Single-Blinded	140	29-86	Adults, palpable cord, extension deficit of at least 20 degrees, MCP joint, single finger.	Prior treatment, CI to CCH treatment anticoagulant therapy, drug/ETOH abuse, chronic neuromuscular disease affecting hand function.	2	CCH injection vs. Needle fasciotomy.
Skov (2017)	RCT	50	>18	Passive extension deficit of 20 degrees or more, well-defined cord, PIP joint	Allergies to CCH, not able to participate in follow up, had received anticoagulant therapy, pregnant or breastfeeding, previous treatment.	3	CCH injection vs. Needle fasciotomy.

## RESULTS

Scherman et al. (2018) were the authors of a two-center randomized control trial that investigated the recurrence rate of treated primary DD contractures after 3 years.<sup>5</sup> This was a

continuation from a previous RCT performed by the same authors in 2016.<sup>5</sup> It compared the use of PNF to collagenase injection in the treatment of Dupuytren's contractures, with evaluations being performed at 3 months, and 1-year.<sup>5</sup> Patients were considered for this study if they: were diagnosed with primary Dupuytren's disease, had a palpable cord, and a PED between 30 and 135 degrees.<sup>5</sup> Exclusion criteria included involvement of the thumb and an extension deficit less than 30 degrees.<sup>5</sup> The digit treated varied upon the extent of contracture, with the most severe digit being selected for the procedure.<sup>5</sup> Patients randomized to CCH injection underwent the procedure according to standard manufacturer protocols and returned to the procedure 24-72 hours later to receive manipulation.<sup>5</sup> This was performed with the use of a median, or ulnar nerve block.<sup>5</sup> Those who were randomized to PNF treatment were brought to a treatment room where aseptic technique was used to perform subdermal injection and perforation of the cord with a 19-gauge needle.<sup>5</sup> Local anesthetic was administered for pain control. A total of 40 digits were treated with CCH injection, and 46 with needle fasciotomy.<sup>5</sup> After 3 years only 40 of the needle fasciotomy group, and 36 of the CCH group were available for follow up.<sup>5</sup> One patient from each group died and the remaining patients lost to follow up had been retreated prior to the 3-year mark.<sup>5</sup>

Scherman et al. defined recurrence of an increase in the PED of 30 degrees or more from the 3-month evaluation point, or if the patient had been retreated.<sup>5</sup> Of the 36 CCH injection patients available for follow up, 12 had a recurrence compared to 17 of the 40 PNF treatment group. Based on these outcomes, there was no proven statistically significant difference found in the recurrence rate between CCH injection and needle fasciotomy. The reported calculated P-value demonstrates this at 0.65, with the set value of significance at <0.05.



**Table 2. 3 Year Recurrence Rate of CCH vs. PNF Treatment (Data from Scherman et al.<sup>5</sup>)**

Outcome	CCH Injection (n=36)	Percutaneous Needle Fasciotomy (n=40)	P-value
Recurrence Rate *	12	17	0.65**
*Recurrence is defined as a passive extension deficit of greater than 30 degrees of the treated joint or needing retreatment prior to 3-year follow up. **Significant P-Value <0.05.			

**Table 3. 3 Year Contracture Prevention Outcomes Post CCH/PNF Treatment (Data from Scherman et al.<sup>5</sup>)**

Experimental Event Rate (EER)	.333
Control Event Rate (CER)	.425
Relative Risk Reduction (RRR)	.214
Relative Benefit Increase (RBI)	.091
Numbers Needed to Treat (NNT)	11.

Stromberg et al. (2016) conducted a single-blinded, single-center, randomized study on a patient population totaling one hundred and forty patients with a single digit contracture involving the MCP joint.<sup>6</sup> Patients were enrolled if they had a contracture greater than 20 degrees in the affected finger and met the additional inclusion/exclusion criteria seen in Table 1. The purpose of this study was to compare the efficacy of CCH to PNF. 69 patients were randomized to CCH injection, 71 to needle fasciotomy.<sup>6</sup> Randomization was done via computer-generated randomization.<sup>6</sup> CCH injection was performed in an outpatient procedure center, under sterile conditions and according to manufacturer instructions.<sup>6</sup> Once the injection was complete, the hand was bandaged, and patients were instructed to avoid using the hand until the following day. Patients returned to the clinic the next day for the treated finger to be manipulated under local anesthesia to disrupt the cord.<sup>6</sup> The treatment protocol for needle fasciotomy included sterile preparation of the hand, administration of local anesthesia, followed by repetitive movements of the needle through the cord until rupture was achieved.<sup>6</sup> These procedures were performed by a single hand surgeon. Both treatment groups received teaching on passive extension exercises to

use at home.<sup>6</sup> Follow-up was performed at 1 week and 1 year where a single physiotherapist examined and measured post-treatment extension deficits with a goniometer.<sup>6</sup> For continuity within this EBM review, only 1-year results will be examined. After 1 year only two patients were lost to follow up, both belonging to the CCH treatment group.<sup>6</sup> One patient cited moving as the barrier to follow up, the other simply declined participation.<sup>6</sup> This study defined recurrence as a passive extension deficit greater than 20 degrees post-treatment.<sup>6</sup> One patient from each treatment group experienced a recurrence of their contracture at the 1-year mark after an initial deficit of fewer than 5 degrees had been achieved.<sup>6</sup>

Based on the treatment results in this study there was no statistically significant difference in outcomes between these two treatment groups. This can be shown by a p-value of  $>0.05$ . In addition to a non-significant p-value, the numbers needed to treat was calculated to be 1000 (NNT:1000) demonstrating a small net effect in the prevention of contracture recurrence.

**Table 4. Recurrence Rate at 1-Year Follow-up between CCH and PNF (Data from Stromberg et al.<sup>6</sup>)**

Parameter	Collagenase Treatment Group (n=67)	PNF Treatment Group (n=71)	P-Value
Recurrence of MCP contracture*	1 (1.7%)	1 (1.6%)	$>0.05^{**}$
*Recurrence is defined as a passive extension deficit of greater than 20 degrees of the treated joint. **Significant P-Value $<0.05$			

**Table 5. 1 Year Contracture Prevention Outcomes Post-CCH, PNF Treatment (Data from Stromberg et al.<sup>6</sup>)**

Experimental Event Rate (EER)	.017
Control Event Rate (CER)	.016
Relative Risk Reduction (RRR)	.059
Relative Benefit Increase (RBI)	.001
Numbers Needed to Treat (NNT)	1000.

Skov et al. (2017) performed a study that compared the treatment of PIP joint contractures by PNF or CCH injection. This was a single-center, independent, randomized controlled trial that followed fifty patients over two years to determine the efficacy of these treatment modalities in DD.<sup>7</sup> Patients were determined eligible for inclusion in the study provided they had a PIP joint contracture with a PED deficit of 20 degrees or more, were 18 years or older, and met the additional inclusion/exclusion criteria available in Table 1.<sup>7</sup> This study group was similar regarding baseline characteristics, however, digits that were affected varied. 21 patients were randomized to PNF, 29 to CCH injection.<sup>7</sup> Randomization of treatment was accomplished by having patients draw envelopes that were prepared using a randomization algorithm.<sup>7</sup> Percutaneous needle fasciotomy was performed by prepping the hand with a topical disinfectant, sterile draping, administration of local anesthetic followed by repetitive perforation of the cord with a 25-gauge needle.<sup>7</sup> This is performed at a slow pace while using passive extension to appropriately visualize the cord and avoid nerve damage. CCH injection was administered under the same sterile conditions according to the manufacturer's guidelines.<sup>7</sup> These patients returned the next day for manipulation to disrupt the cord. All patients were given instructions to remove bandages after 24 hours and were fitted for an orthotic device to wear at night during the first 4 months.<sup>7</sup> Study participants were instructed to follow up in 30 days, 1 year, and 2 years for evaluation and clinical measurements performed by a nurse.<sup>7</sup> Measurement of PED was performed with a goniometer. At 1-year post-treatment, 3 patients were lost to follow up in the CCH treatment group. All PNF patients were seen after 1 year for examination.<sup>7</sup> This study used a PED measurement of 20 degrees or more to define a recurrence of contracture. While data is available for the evidence of contracture recurrence at 30 days, 1 year and 2 years, only the 1-year results will be examined for this review. Between the two treatment groups, 65%

of those treated with CCH had contracture recurrence, compared to 57% who received PNF.<sup>7</sup>

This demonstrates a similar rate of recurrence after being treated with either CCH or PNF. The statistical significance of these results can be deemed non-significant, denoted by the P-value of .56, indicating a small treatment effect.<sup>7</sup>

**Table 6. 1 Year Recurrence Rate of CCH vs. PNF Treatment (Data from Skov et al.<sup>7</sup>)**

Outcome	CCH	PNF	P-Value
Contracture Recurrence* (n=47) (95% CI)	65% (46-85)	57% (35-79)	.56**
*Recurrence is defined as a passive extension deficit >20 degrees			
** Significant P-Value <0.05			

**Table 7. 1 Year Contracture Prevention Outcomes Post-CCH, PNF Treatment (Data from Skov et al.<sup>7</sup>)**

Experimental Event Rate (EER)	.650
Control Event Rate (CER)	.570
Relative Risk Reduction (RRR)	.140
Relative Benefit Increase (RBI)	.08
Numbers needed to Treat (NNT)	NNT=13

## DISCUSSION

Dupuytren's disease is a common connective tissue disorder that is irreversible. The resulting contractures may lead to a patient's impaired ability to perform the tasks of everyday life. Things such as perform certain occupations, prepare food, write with a pen, or button a sweater. While there are treatments available, there is currently no cure for the disease. Due to the high recurrence rates of these contractures, recurrence is a noteworthy area of research and a valid outcome for patients to consider when deciding among the various treatments for DD. All three studies used in this review compared CCH injection to PNF on adult patients with a 1, or 3-year follow up. Of the three RTCs reviewed, all authors reported a p-value >0.05. This demonstrates no statistically significant difference between these two treatments in the rate of contracture recurrence.

A limitation seen within this review is the variance of digits and joints being treated in these studies. Stromberg et al. exclusively enrolled patients with an MCP contracture, Skov et al. selected those with PIP contractures, and Scherman et al. accepted a combination of the two.<sup>5-7</sup> This may be pertinent due to the understanding that PIP joints and ulnar digits are more resistant to treatment. Another limitation was the lack of blinding in the individuals assessing a patient post-treatment. Stromberg et al. was the only study where the physiotherapist performing clinical measurements was blinded to which procedure the patient received.<sup>6</sup> Other limitations include small sample size, variability when performing clinical measurements, and non-blinding to treatment.

Collagenase injection is a new, FDA approved non-surgical treatment designed to weaken the fascial cords causing the contracted digits. CCH has become increasingly used in the treatment of Dupuytren's contractures and is available throughout the U.S. and Europe, marketed under the name Xiapex. While there is good evidence for the efficacy of CCH injection in reversing extension deficits, its cost-effectiveness should be taken into consideration. During the trial Stromberg et al. performed, the overall cost of CCH injection is \$1,410, compared to \$530 for needle fasciotomy.<sup>6</sup> Along with the proposed increase in cost, CCH injection requires a second clinic visit for manipulation, which may be burdensome to patients. Needle fasciotomy has been the standard minimally invasive treatment modality, is less costly than CCH injection; however, it poses a slightly increased risk of nerve damage.<sup>6</sup> As with most injection procedures such as CCH and PNF, adverse events may include infection, nerve damage, bleeding, and hematoma formation.

## **CONCLUSION**

Based on the analysis of three randomized controlled trials, there is no significant difference in the rate of contracture recurrence between CCH injection and PNF. All three studies concluded there was no outcome difference, in terms of recurrence rates when compared against each other during clinical trials. Future studies may be improved by increasing sample size, and blinding evaluators to the patient's mode of treatment to prevent bias. Contracture recurrence is a valid outcome to consider when deciding on a treatment plan for DD. However, exploring other patient-oriented outcomes such as cost, risk of adverse events, number of visits required, and patient satisfaction may be more advantageous in the comparison of CCH to PNF.

## REFERENCES

1. Lanting R, Broekstra DC, Werker PM, Van den Heuvel ER. A systematic review and meta-analysis on the prevalence of dupuytren disease in the general population of western countries. *Plast Reconstr Surg*. 2014;133(3):593-603. doi:10.1097/01.prs.0000438455.37604.0f.
2. Camper SB, Divino V, Hurley D, DeKoven M. Cost per episode of care with collagenase *costridium histolyticum* versus fasciectomy for dupuyten contracture: A real-world claims database analysis. *J Hand Surg A Global Online*. 2019;1(11):57-64. doi: <https://doi.org/10.1016/j.jhsg.2018.12.005>. Accessed October 4, 2020.
3. Salari N, Heydari M, Hassanabadi M, et al. The worldwide prevalence of the Dupuytren disease: A comprehensive systematic review and meta-analysis. *J Orthop Surg Res*. 2020;15(1):495. Published 2020 Oct 28. doi:10.1186/s13018-020-01999-7
4. Macaulay D, Ivanova J, Birnbaum H, Sorg R, Skodny P. Direct and indirect costs associated with dupuytren's contracture. *J Med Econ*. 2012;15(4):664-671. doi: 10.3111/13696998.2012.670678.
5. Scherman P, Jenmalm P, Dahlin LB. Three-year recurrence of dupuytren's contracture after needle fasciotomy and collagenase injection: A two-centre randomized controlled trial. *J Hand Surg Eur Vol*. 2018;43(8):836-840. doi: 10.1177/1753193418786947.
6. Stromberg J, Ibsen-Sorensen A, Friden J. Comparison of treatment outcome after collagenase and needle fasciotomy for dupuytren contracture: A randomized, single-blinded, clinical trial with a 1-year follow-up. *J Hand Surg A*. 2016;41(9):873-880. doi: 10.1016/j.jhsa.2016.06.014.
7. Skov ST, Bisgaard T, Sondergaard P, Lange J. Injectable collagenase versus percutaneous needle fasciotomy for dupuytren contracture in proximal interphalangeal joints: A randomized controlled trial. *J Hand Surg Am*. 2017; 42(5):321-328.e3. doi: S0363-5023(16)30817-6.