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Original Research

Clinical Outcomes of Collagenase Injections in Management of Dupuytren Contracture of the Proximal Interphalangeal Joint



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Purpose: Dupuytren contracture is characterized by the formation of cords and nodules in the palm. Surgical release has historically been the definitive treatment. Collagenase clostridium histolyticum (CCH) has been used successfully as an alternative to surgery. The treatment of proximal interphalangeal (PIP) contractures is the most challenging. The purpose of this study was to evaluate CCH treatment for Dupuytren contracture of the PIP joint.

Methods: A retrospective chart review was performed for CCH treatment of Dupuytren contracture at a single institution from January 2010 to April 2023. Data collected included pretreatment/posttreatment total flexion contracture and adverse events. Contractures were analyzed both by severity (high >40° and low <40°) and type (isolated PIP; combined metacarpophalangeal and PIP).

Results: A total of 304 patients with 470 PIP joints treated were included. Digits with isolated and combined contractures each had an average pre-CCH treatment contracture of 51 (±23) degrees. Post-manipulations the contractures were 6 (±13) and 7 (±16) degrees, respectively. Clinical success (<5° residual contracture) and improvement (>50% correction of contracture) were associated with low severity contractures at postmanipulation. There were 256 adverse events recorded (54.5%), including 187 skin tears (39.8%), 68 cases of lymphadenopathy (14.5%), and one injection site infection (0.2%). High severity and combined contractures were independently associated with an increased incidence of skin tears upon manipulation.

Conclusions: Collagenase clostridium histolyticum treatment is effective for isolated or combined PIP joint contractures. Adverse events were associated with more severe contractures. Given the degree of improvement based on contracture severity, earlier intervention may provide better correction of contracture.

Type of study/level of evidence: Therapeutic III.

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Dupuytren contracture (DC) is a benign, progressive, fibroproliferative disorder involving the formation of nodules and cords in the palmar and digital fascia. The normal fascia of the palm and digits develop nodules and cords that over time cause fixed flexion contractures to develop at both the metacarpophalangeal (MCP)

and proximal interphalangeal (PIP) joints, causing loss of function and disability.¹

Surgical options, including limited fasciectomy, have a long-term recurrence rate of contractures ranging from 4% to 73%.^{2–7} Surgical complications include infection, stiffness, hematoma, delayed wound healing, neurovascular injury, and complex regional pain syndrome. Revision surgery may be more challenging with higher rates of complications including neurovascular injury.⁸ Percutaneous needle aponeurotomy, an alternative to surgical intervention, has shown comparable results at short-term follow-

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up with adverse events (AEs) including skin tears and rarely nerve injury.^{6,9,10} Collagenase clostridium histolyticum (CCH) is an injectable combination of microbial enzymes selective for types I and III collagen, which was approved for the management of DC by the Food and Drug Administration in 2010.¹¹ Collagenase clostridium histolyticum is injected into the pathologic cord, and the associated joint is manipulated 1–2 days later to facilitate cord rupture.¹² Multiple clinical trials and surveillance studies have demonstrated CCH to be an effective and well-tolerated treatment option.^{13–16} Common AEs following CCH treatment include lymphadenopathy, bruising, swelling, pruritis, and skin tears. Rare AEs include complex regional pain syndrome and flexor tendon rupture.¹⁷

Collagenase clostridium histolyticum treatment has shown to be more effective in treating MCP compared with PIP contractures, with enhanced motion and decreased contracture recurrence rates at the MCP joint.^{18–20} Proposed etiologies of PIP joint contractures are secondary tightening of the collateral ligaments, volar plate contracture, central slip attenuation, and intra-articular adhesions of the PIP joint.^{21–23}

Draviraj and Chakrabarti²⁴ illustrated that PIP joint correction has a greater correlation to hand functional outcomes compared with MCP joints. Proximal interphalangeal contractures often do not occur in isolation, and in the studies investigating multiple joint contractures with CCH treatment, few have compared outcomes with that of single joint contractures.^{25–28} The purpose of this study was to evaluate CCH treatment for DC of the PIP joint including isolated and combined contractures.

Materials and Methods

A retrospective chart review was conducted of patients with CCH treatment for DC by six fellowship-trained hand surgeons at a single institution from September 2010 to April 2023. All patients with one or more PIP joints with CCH treatment were included. Multiple cords were treated when clinically indicated. Patients had an hand therapy visit postmanipulation where they were fitted for a night orthosis. Patients were excluded for severe boutonniere deformity, intrinsic contractures, or if contracture measurements were not obtained. Patients who received multiple injections for treatment of the same joint were recorded in two ways. If the same digit and target joint were treated with a repeat injection of CCH within 3 months because of insufficient correction, then this was considered a serial treatment. If the repeat CCH treatment occurred after 3 months, then it was recorded as an independent event. Primary outcome measure was the degree of contracture correction after CCH treatment. Proximal interphalangeal contractures were further compared based on if they occurred in isolation (isolated PIP) or were associated with an MCP contracture on the same digit (combined PIP and MCP). Data collected included demographics, pretreatment and posttreatment PIP flexion contracture and AE at 4 and 12 weeks. Proximal interphalangeal contractures were further stratified into high (>40° contracture) and low severity groups (≤40° contracture) based on outcomes of the CORD I/II trials.^{15,29} Outcomes were classified into clinical success (<5° residual contracture) or clinical improvement (>50% contracture improvement from pretreatment).^{15,29} This study was approved by the Institutional Review Board.

Statistical analyses were performed using SPSS (IBM SPSS Statistics for Windows, v28: IBM Corp). Continuous variables reported as means and SD were analyzed using paired Student *t* tests or independent Student *t* tests, where appropriate. Categorical variables, reported as proportions, were compared using chi-square or Fisher exact tests, where appropriate. An a priori power analysis (80%, $\alpha = 0.5$) was performed to determine a minimal sample size

Table 1
Patient Demographics*

Number of Patients	304	(%)
Sex		
Male	246	80.9
Female	58	19.1
Joints per hand		
Left	228	48.5
Right	242	51.5
Total digits treated		
Total	470	
Index	21	4.5
Long	46	9.8
Ring	128	27.2
Small	275	58.5

DC, Dupuytren contracture.

* Overall demographics and digits affected by DC.

to detect an effect of treatment (minimum 40° of improvement) and to detect a 10° difference in contracture correction in a group comparison.^{5,15} A minimum of 107 patients per group were needed. All tests were two-sided with alpha set at 0.05.

Results

A total of 481 patients with DC who received CCH treatment were identified. After exclusion, 304 patients with 470 PIP joints were included in the final analysis. Fourteen patients underwent serial treatment. One patient had three rounds of treatment. Demographic characteristics and digits treated are listed in Table 1.

A summary of pretreatment contracture characteristics and response to CCH treatment for PIP joints, as well as further subdivisions by contracture severity and type, are listed in Table 2. Average posttreatment flexion contracture was $6.4 \pm 14.9^\circ$, representing an average improvement of $44.4 \pm 24.8^\circ$ ($P < .05$). There was a total of 136 (28.9%) isolated PIP contractures and 334 (71.1%) combined PIP contractures. Average pretreatment flexion contracture at the PIP joint was 50.7 ± 22.9 for isolated joints and $50.8 \pm 27.4^\circ$ for combined joints. Average postmanipulation contracture was $6.1 \pm 12.8^\circ$ for isolated and $6.6 \pm 15.7^\circ$ for the combined PIP joints group, for a mean improvement of $44.6 \pm 20.8^\circ$ and $44.3 \pm 26.3^\circ$, respectively ($P < .05$ for both groups). There was no significant difference in the correction between contracture types ($P = .945$; $P = .746$, respectively). Clinical success and clinical improvement were greater with the low severity group ($P < .05$, for each; Table 3).

Adverse events occurred in 256 patients (54.5%), including 187 skin tears (39.8%), 68 cases of lymphadenopathy (14.5%), and one possible superficial skin infection (improved with local care) (0.2%). Skin tears were appropriately dressed and allowed to heal by secondary intention. High contracture severity and combined contracture type were independently associated with the occurrence of skin tears ($P < .05$, for each). There was no association between contracture severity or type and occurrence of lymphadenopathy. No flexor tendon ruptures occurred.

Discussion

Our results demonstrate that CCH treatment provides improvement of contracture for isolated and combined PIP joint contractures. Clinical success and improvement were significantly associated with the low severity group.

Badalamente et al³⁰ demonstrated clinical success and improvement at 30 days following the first PIP CCH treatment in 27% and 49% of PIP joints and 34% and 58% after the final treatment.

Table 2
PIP Joint Contracture Characteristics*

		Preinjection	Postmanipulation	Postmanipulation Change in Contracture
		Average ± SD	Average ± SD	Average ± SD
Flexion contracture (n) in degrees	Total (470)	51 ± 26	6 ± 15	44 ± 25 [†]
Flexion contracture (n) by severity in degrees	High (257)	70 ± 19	10 ± 19	59 ± 24 [†]
	Low (213)	28 ± 12	2.0 ± 5	27 ± 12 [†]
Flexion contracture (n) by type in degrees	Isolated (136)	51 ± 23	6 ± 13	45 ± 21 [†]
	Combined (334)	51 ± 27	7 ± 16	44 ± 26 [†]

PIP, proximal interphalangeal; MCP, metacarpophalangeal.

* PIP joint contracture baseline contracture characteristics, postcollagenase injection and manipulation, and at most recent follow-up, further stratified by type and severity. High and low severity contractures are those preinjection contractures that are >40° and ≤40°, respectively. Isolated and combined contractures are those contractures that are isolated to the PIP joint, or those that have an associated MCP joint contracture of the treated digit.

[†] Denotes comparison of means with a *P* value < .001.

Table 3
PIP Clinical Success and Clinical Improvement by Initial Severity and Joint Type

		High Severity	Low Severity	Isolated	Combined	Totals
Clinical success postmanipulation	Yes (%)	176 (68.5)	194 (91.1)*	105 (77.2)	265 (79.3)xxx	370 (78.7)
Clinical improvement postmanipulation	Yes (%)	237 (92.2)	209 (98.1)*	131 (96.3)	315 (94.3)xx	446 (94.9)

Clinical success for treated joints is defined as treatment of contracture to ≤5°, while clinical improvement is defined as correction to ≤50% of original contracture. Chi-square were performed for all comparisons.

* = *P* < .05; xx → *P* = .369; xxx → *P* = .608.

These authors reported on average 1.6 injections per joint treated, allowing for up to three injections if clinical success was not achieved after 30 days. We achieved a higher short-term clinical success and improvement following just one round of treatment. Our 14 patients who received serial treatments similarly achieved clinical success. If residual contracture is present after initial treatment with functional impairment, patients may elect repeat treatment.³¹

Our results corroborate known difficulties with PIP joint correction. The higher clinical success rate in the low versus high severity group highlights this limitation. Chronic DC often involves contracture of the volar plate, collateral ligaments, and central slip attenuation that hinders PIP correction. This knowledge can provide a basis to counsel patients on their expected improvement based on the severity of contracture.^{21–23} Proximal interphalangeal correction with CCH treatment must be compared against the other available treatment modalities. Povlsen B and Povlsen SD³² compared 10 CCH patients with 10 patients treated surgically. Proximal interphalangeal total active range of motion was superior in the CCH group for both isolated PIP contractures and combined contractures, whereas MCP improvement alone was superior in the surgical group.³² Weakness of their study included low enrollment, unquantified follow-up, and no discussion of complications or AEs. Additionally, our overall treatment success of 79% improvement for PIP joints compares favorably with the study by van Rijssen et al³³ who found correction to <5° via limited fasciectomy and needle fasciotomy in 47% and 26% of patients, respectively.

Coleman et al³⁴ investigated CCH treatment effectiveness in 60 patients with combined contractures on the same finger or two MCP joints. Initial Food and Drug Administration approval allowed one cord to be injected at 30-day intervals.^{29,30,34} However, DC patients had an average of three affected joints during the previous CORD I/II and JOINT I/II trials.^{15,17,29,35} Coleman et al³⁴ demonstrated reductions in mean total flexion contracture, increases in mean total active range of motion, and similar incidence of severe AEs. There were 86% and 66% decreases in MCP and PIP joint contractures, respectively, consistent with the CORD I trial.²⁹ In summary, concurrent CCH treatment for multiple DCs of a single finger or hand showed similar improvements at 30-day follow-up compared with single joint injections. We found there was no

statistical difference in the mean correction achieved at the PIP joint between isolated and combined groups (*P* = .746).

Adverse events recorded in our study included 68 cases of lymphadenopathy (14.5%) and 187 skin tears (39.8%). No major AEs were observed. Zhou et al⁵ evaluated patients undergoing CCH treatment and limited fasciectomy and reported significantly fewer AEs (five skin tears [8%] and two cases of lymphadenopathy [3%]) compared with surgical release. Other reports of AEs have described rates of skin tears that range from 18.4% to 27% and rates of lymphadenopathy as high as 16%.^{18,27,28} Although our incidence was higher than previously published studies, all skin tears healed without further complication.

Limitations of our study include the lack of documentation of chronicity of contracture, patients excluded because of the lack of complete documentation, and limitations on follow-up.

Collagenase clostridium histolyticum treatment may provide improvement for both combined and isolated PIP joint contractures. Given more severe contractures have higher rates of AEs, earlier intervention may provide better clinical outcomes.

Conflicts of Interest

Dr Nydick reports support from Endo (education research grant) and association or financial involvement with Trimed, Axogen, Endo, and Conmed. No benefits in any form have been received or will be received by the other authors related directly to this article.

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