Does Use of a Night Extension Orthosis Improve Outcomes in Patients With Dupuytren Contracture Treated With Injectable Collagenase?

Nathan Lorris Bowers, MD, * Gregory Alan Merrell, MD, † Todd Foster, PhD, ‡ F. Thomas D. Kaplan, MD  

* Indiana University, Indianapolis, IN  
† Indiana Hand to Shoulder Center, Indianapolis, IN  
‡ St. Vincent Hospital, Indianapolis, IN

Purpose: Current prescribing information for the treatment of patients with Dupuytren contracture with injectable collagenase Clostridium histolyticum (CCH) recommends use of a night extension orthosis for 4 months after treatment. The present study examines whether this treatment improves the outcomes.

Methods: Adult patients with Dupuytren contracture treated with CCH during the study period were eligible for inclusion. The patients were randomized to orthosis or no orthosis groups and were stratified based on the severity of contracture prior to randomization. The orthosis group was fitted post-manipulation with a hand-based custom orthosis that held the treated finger in maximal comfortable extension, and the patients were instructed to wear the orthosis at night for 3 months. The patients were assessed at 7–10 days, 30 days, and 90 days postmanipulation. Orthosis compliance was measured with a survey. The primary outcome measure was improvement in total active extension (TAE), defined as the sum of active metacarpophalangeal (MCP), proximal interphalangeal, and distal interphalangeal joint extension in the treated finger at 90 days after treatment. Secondary outcomes included total active flexion (TAF), Michigan Hand Questionnaire scores, patient satisfaction, and clinical success.

Results: Twenty-six patients completed the study, 12 in the orthosis group and 14 in the no orthosis group. The majority of contractures (90%) were primarily through the MCP joint. The patients in both groups demonstrated significant improvements in TAE at 90-day follow-up (orthosis P = .002, no orthosis P = .001). The difference in improvement in the median TAE between the 2 groups was not significant (P = .40). There were no significant differences between groups for TAE, TAF, Michigan Hand Questionnaire scores, patient satisfaction, or clinical success at any of the time points assessed (P > .05).

Conclusions: In patients with Dupuytren contracture with primarily MCP joint involvement, providing an orthosis after treatment with CCH may not offer a short-term benefit compared with CCH treatment alone in terms of TAE, TAF, or patient-reported outcome measures.

Type of study/level of evidence: Therapeutic I.

Dupuytren contracture is a benign fibroproliferative disorder of the palmar fascia in which excessive collagen deposition forms cords that may progress to finger flexion contractures that often interfere with hand function.1 Injectable collagenase Clostridium histolyticum (CCH) was approved by the United States Food and Drug Administration in 2010 and by the European Medicines Agency in 2011 as a nonsurgical alternative for the treatment of adults with Dupuytren contracture and a palpable cord.2 Collagenase C. histolyticum (0.58 mg) is injected into the cord identified as causing the contracture of the metacarpophalangeal (MCP) or proximal interphalangeal (PIP) joint, and the finger is passively manipulated into extension to rupture the cord. Following the manipulation, the current prescribing information instructs the hand surgeon to “fit the patient with a splint and provide instructions for use at bedtime for up to 4 months to maintain finger extension.”3 Additionally, the patient is instructed to perform hand therapy that includes finger flexion and extension exercises to maintain their extension.4–6

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Corresponding author: F. Thomas D. Kaplan, MD, Indiana Hand to Shoulder Center, 8501 Harcourt Rd, Indianapolis, IN 46260.  
E-mail address: TKaplan@htscc.com (F.T.D. Kaplan).

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One retrospective study investigated orthosis use after needle aponeurotomy for the treatment of Dupuytren contracture and demonstrated no significant difference in the gains of PIP or MCP joint range of motion (ROM) in patients treated with a night orthosis and hand therapy compared with those treated with hand therapy alone. Several previous studies have investigated the efficacy of orthosis use after open fasciectomy. Two retrospective studies demonstrated no significant difference in ROM or a detrimental effect to finger ROM from orthosis use after fasciectomy. One retrospective study showed statistically significant improvement in PIP joint extension in patients compliant with an orthosis after fasciectomy. Three randomized trials demonstrated no benefit to finger ROM or patient-reported outcome scores from orthosis use and hand therapy compared with hand therapy alone. Because of the mixed results of these studies on the benefits of night orthosis use after the treatment of Dupuytren contracture with other modalities and the dearth of literature on the necessity of orthosis use after the treatment of Dupuytren contracture with CCH, we hypothesized that there was no benefit in the use of a night extension orthosis following treatment with CCH for Dupuytren contracture.

Materials and Methods

This study was a prospective randomized controlled trial (RCT) conducted at a single institution in the United States. The study was approved by the institutional review board of Ascension St. Vincent. All patients provided written informed consent to participate in the trial and were free to withdraw at any time.

All adult patients with Dupuytren contracture and a palpable cord treated with CCH by the primary investigator (28 patients) or his designee (1 patient) from February 2018 to January 2020 were screened for inclusion in the study (Fig. 1). The patients were excluded from the trial if they had prior treatment of Dupuytren contracture (dermofasciectomy, fasciectomy, or needle aponeurotomy) in the finger to be treated with CCH or if they declined participation in the study. Twenty-nine patients were enrolled in the study (28 men and 1 woman). After informed consent was obtained, a complete medical history was recorded in addition to baseline Michigan Hand Outcomes Questionnaire (MHQ) scores and Visual Analog Scale (VAS) pain scores. Baseline finger goniometry was performed on all fingers of the affected hand by the treating physician.

The patients were stratified, based on the severity of baseline contracture, to either low severity (<50° contracture) or high severity (≥50° contracture). They were then randomized in a 1:1 ratio for each severity group to orthosis or no orthosis groups using a computer-generated random number table.

All patients received 1 dose of 0.58-mg CCH, injected into the cord causing the contracture, per manufacturer’s guidelines. After injection, hands were placed in a soft, bulky dressing, and the patients were instructed to keep their hand elevated until their scheduled follow-up. At the second visit, 2–3 days following CCH injection, the treated finger was injected with local anesthetic in the midpalm and manipulated into extension. Goniometry was performed on the treated finger following manipulation. The patients randomized to the orthosis group were placed into a thermoplastic orthosis custom fabricated by a hand therapist. The orthosis was molded on the palmar surface of the hand, holding the treated finger in maximum comfortable extension. The patients in the orthosis group were instructed to wear the orthosis during sleep for 3 months, and those in the no orthosis group were placed into a soft dressing and instructed to remove it the next day. All patients were instructed about active tendon gliding ROM exercises, active and passive stretching, and edema control by a hand therapist. The patients performed therapy on their own at home and were reassessed by the hand therapist at each follow-up visit, as necessary.

The patients were assessed at approximately 7–10 days, 30 days, and 90 days after manipulation. The ROM of each joint in the treated finger was measured with a goniometer by the primary investigator or his designee, who was trained to perform finger goniometry in a consistent manner. Measurements were taken for the MCP, PIP, and distal interphalangeal joints in each patient regardless of the joint primarily treated. The patients completed a self-administered MHQ, VAS, and satisfaction survey at each subsequent visit. Orthosis compliance in the orthosis group was measured with a survey given at each follow-up visit. The primary endpoint of the study was total active extension (TAE), defined as the sum of active MCP, PIP, and distal interphalangeal joint extension, in the treated finger at 3 months after the treatment. Higher values indicated greater contracture, and a value of 0° indicated full active extension; hyperextension was not recorded. Total active extension was chosen as the primary outcome because cords may affect additional joints in addition to the primarily treated joint contracture. Additionally, TAE captured the beneficial or deleterious effects of orthosis fabrication on the adjacent joints of the finger following treatment. Secondary endpoints included MCP extension, PIP extension, total active flexion (TAF), VAS scores, MHQ scores, patient satisfaction, orthosis compliance, and clinical success at 3 months after the treatment. Clinical success for the treatment of Dupuytren contracture with CCH was defined as the reduction of contracture in the treated joint to within 5° of full extension. Sample size estimates for noninferiority were conducted for the primary outcome of TAE. A priori power calculations using an alpha of 0.05 and power of 90% determined that 11 patients would be needed per group. Goal enrollment was set at 30 total patients to allow for dropout and examination of secondary outcomes. No power analysis was performed for secondary outcomes. Data were analyzed based on intention to treat principal. Medians were selected for the comparisons between groups to allow for a more accurate presentation of the data with a limited number of patients. Nevertheless, means are also presented for TAE, PIP, and MCP extension to allow facile interpretation with previously published research. Fisher exact test was used to compare categorical variables among the groups. Mann-Whitney U test or Wilcoxon signed-rank test were used to compare changes in continuous variables between groups and between time points for each patient, respectively. IBM SPSS Statistics for Windows 24.0 was used to complete all inferential tests.

Results

Twenty-nine patients were enrolled in the study, 14 in the orthosis group and 15 in the no orthosis group. Two patients in the orthosis group and 1 patient in the no orthosis group completed only the 30-day follow-up. The full 90-day follow-up was completed by 90% of patients, 12 in the orthosis group and 14 in the no orthosis group. There were no significant differences in baseline sex, age, race, age at onset of Dupuytren contracture, and digit involvement (P > .05) (Table 1). The majority of cords treated in the study primarily affected the MCP joint (26 of 29 cords, 90%), with 3 of 29 cords primarily affecting the PIP joint. In the orthosis group, 79% of the cords primarily affected the MCP joint, and 21% primarily affected the PIP joint. In the no orthosis group, 100% of the cords
primarily affected the MCP joint ($P < .001$). Several patients in each group with primary MCP joint contractures also had concomitant contractures of the PIP joint, which were not specifically treated. There was no statistically significant difference in the median PIP joint contracture between the groups ($P = .21$). Mean baseline PIP joint contracture was 21° in the orthosis group and 7° in the no orthosis group. There were no significant differences among the groups regarding baseline median values in TAE, TAF, MCP extension, MHQ, or VAS scores ($P > .05$) (Table 2).

The patients in both the groups demonstrated statistically significant improvements in TAE at the 90-day follow-up compared with the baseline values. The mean TAE at 90 days was 11° (improvement of 53°) ($P = .002$) in the orthosis group and 9° (improvement of 46°) ($P = .001$) in the no orthosis group. The median difference in improvement in TAE at 90 days between the 2 groups was not significant ($P = .40$). All the patients in the orthosis group and 93% of patients in the no orthosis group had >50% improvement in TAE at 90 days ($P > .99$). Mean MCP extension at 90 days was 1° in the orthosis group (improvement of 41°) and 2° (improvement of 45°) in the no orthosis group. Mean PIP extension at 90 days was 9° (improvement of 12°) in the orthosis group and 7°

| Characteristic                  | Orthosis Group (n = 14) | No Orthosis Group (n = 15) | $P$ value |
|--------------------------------|-------------------------|---------------------------|-----------|
| Male, n (%)                    | 13 (93%)                | 15 (100%)                 | .48       |
| Female, n (%)                  | 1 (7%)                  | 0 (0%)                    | .002      |
| High severity ($>50°$), n (%)  | 8 (57%)                 | 6 (40%)                   | .47       |
| Low severity                   | 6 (43%)                 | 9 (60%)                   | .84       |
| White race                     | 14 (100%)               | 15 (100%)                 | >.99      |
| Median age                     | 52                      | 55                        |           |
| Little finger, n (%)           | 7 (50%)                 | 6 (40%)                   | .19       |
| Cord primarily affecting MCP, n (%) | 11 (78%)               | 15 (100%)                 | <.001     |

Figure 1. CONSORT 2010 flow diagram. Adult patients with Dupuytren contracture and a palpable cord treated with CCH by the primary investigator (28 patients) or his designee (1 patient) from February 2018 to January 2020 were screened for inclusion in the study.
follow-up, which included all enrolled patients, was not significantly different between the 2 groups. The orthosis group had a median TAE of 10 (11) compared with the no orthosis group of 5 (9) (P = .084) (Table 3). Three patients, 2 in the orthosis group and 1 in the no orthosis group, were unable to return for their final 90-day follow-up visit. The difference in the primary endpoint of median TAE at the 30-day follow-up, which included all enrolled patients, was not significantly different between the 2 groups. The orthosis group had a median TAE of 10 (11), and the no orthosis group had a median TAE of 0° (P = .18). The median TAE in each group, ranging from the 25th percentile to the 75th percentile, is displayed in Figure 2. There were no statistically significant differences in the secondary endpoints of median TAF, PIP, and MCP extension, MHQ, or VAS scores at the 30-day follow-up (P > .05) (Table 4).

The patients in both the groups reported high satisfaction with the procedure at the 30-day follow-up. There was no statistically significant difference in patient satisfaction between the 2 groups, (P = .41) (Table 4). Treatment success, defined as the reduction of contracture in the treated joint to within 5° of full extension at the 90-day follow-up, was obtained in 22 of 26 (85%) patients, 9 of 12 (75%) in the orthosis group and 13 of 14 (93%) in the no orthosis group (P = .31) (Table 5).

Of the 12 patients in the orthosis group who completed the 90-day follow-up, 6 patients (50%) reported wearing the orthosis every night for the 90-day period following manipulation. Four patients (33%) reported that they did not wear the orthosis at all in the month preceding their final 90-day follow-up visit. Orthosis compliance was higher earlier in the study; at 7–10-day follow-up, 13 patients (93%) reported wearing the orthosis every night. At the 30-day follow-up, 10 patients (77%) reported wearing the orthosis at least 6 nights per week over the preceding month. The low number of patients in the orthosis group precluded meaningful analysis of the patients who were and were not compliant with orthosis use at night.

**Table 2**
Baseline Measurements

| Baseline Measurement | Orthosis Group (n = 14) | No Orthosis Group (n = 15) | Z (median) | P Value (median) |
|----------------------|-------------------------|---------------------------|------------|-----------------|
| TAE                  | Median (mean)           | Mean 95% CI               | Median (mean) | Mean 95% CI   |
| TAF                  | 58 (64)                 | 48–80                     | 47 (55)    | 43–68          | -0.87       | .38        |
| MCP extension        | 243 (244.86)            | 238–252                   | 240 (238.20)| 230–246       | -1.01       | .31        |
| PIP extension        | 47 (43)                 | 27–59                     | 38 (47)    | 37–56          | 0.00        | >.99       |
| MHQ treated hand     | 15 (21)                 | 8–35                      | 4 (7)      | 3–12           | -1.26       | .21        |
| VAS score            | 76                      | N/A                       | 67         | N/A            | -0.98       | .33        |

N/A, not available.

**Table 3**
Ninety-Day Outcomes

| 90-Day Measurement | Orthosis Group (n = 14) | No Orthosis Group (n = 15) | Z (median) | P Value (median) |
|--------------------|-------------------------|---------------------------|------------|-----------------|
| TAE                | Median (mean)           | Mean 95% CI               | Median (mean) | Mean 95% CI   |
| TAF                | 10 (11)                 | 5–17                      | 5 (9)      | 1–18           | -0.84       | .40        |
| MCP extension      | 247 (250.25)            | 239–262                   | 247 (249.86)| 240–260       | -0.23       | .82        |
| PIP extension      | 0 (1)                   | 0–4                       | 0 (2)      | 0–4            | -0.30       | .77        |
| MHQ Treated Hand   | 76                      | N/A                       | 97         | N/A            | -0.57       | .57        |
| VAS Score          | 5                       | N/A                       | 0          | N/A            | -1.83       | .07        |

N/A, not available.

(no change) in the no orthosis group. There were no significant differences between the median values of the orthosis and the no orthosis groups for TAE, TAF, and MHQ scores at any of the time points assessed (P > .05) (Table 3).

The difference in the primary endpoint of median TAE at the 30-day follow-up, which included all enrolled patients, was not significantly different between the 2 groups. The orthosis group had a median TAE of 10°, and the no orthosis group had a median TAE of 0° (P = .18). The median TAE in each group, ranging from the 25th percentile to the 75th percentile, is displayed in Figure 2. There were no statistically significant differences in the secondary endpoints of median TAF, PIP, and MCP extension, MHQ, or VAS scores at the 30-day follow-up (P > .05).

The patients in both the groups reported high satisfaction with the procedure at the 30-day follow-up. There was no statistically significant difference in patient satisfaction between the 2 groups, (P = .41) (Table 4). Treatment success, defined as the reduction of contracture in the treated joint to within 5° of full extension at the 90-day follow-up, was obtained in 22 of 26 (85%) patients, 9 of 12 (75%) in the orthosis group and 13 of 14 (93%) in the no orthosis group (P = .31) (Table 5).

Of the 12 patients in the orthosis group who completed the 90-day follow-up, 6 patients (50%) reported wearing the orthosis every night for the 90-day period following manipulation. Four patients (33%) reported that they did not wear the orthosis at all in the month preceding their final 90-day follow-up visit. Orthosis compliance was higher earlier in the study; at 7–10-day follow-up, 13 patients (93%) reported wearing the orthosis every night. At the 30-day follow-up, 10 patients (77%) reported wearing the orthosis at least 6 nights per week over the preceding month. The low number of patients in the orthosis group precluded meaningful analysis of the patients who were and were not compliant with orthosis use at night.

**Discussion**

We investigated the effects of providing a night extension orthosis to patients over 3 months following the treatment of Dupuytren contracture with injectable CCH. Our analysis demonstrated no significant improvement in short-term TAE in patients provided with an extension orthosis for night use in a population of patients with primarily MCP joint contractures.

Regarding our primary endpoint, TAE, the study revealed that providing the patients with a night extension orthosis may provide no benefit on TAE at 90 days following treatment compared with home exercises alone. The results of the present study mirror 3 RCTs performed on the effect of night extension orthoses after treatment of Dupuytren contracture with surgical fasciectomy.11–13 Collins et al.12 performed a randomized controlled trial of 56 patients treated with surgical release of Dupuytren contracture. Twenty-six patients received static extension splints to be worn at night for 6 months. At the 12-month follow-up, they found no significant difference in TAE, TAF, grip strength, or Disability of the Arm, Shoulder and Hand scores.12 Jerosch-Herold et al.11 performed a multicenter study of 154 patients randomized to receive extension splints to be worn at night for 6 months in addition to hand therapy or to receive hand therapy alone. At 1 year after surgery, there was no significant difference in the groups’ total extension deficit, Disability of the Arm, Shoulder and Hand scores, or satisfaction scores.11 Kemler et al.13 randomized 54 patients with PIP joint contractures of 30° or more to directly-supervised hand therapy alone or supervised therapy with a 3-month orthosis protocol. At 1 year after surgery, they demonstrated no significant difference in the reduction of flexion contracture.13 Our results are also consistent with data on the lack of efficacy of night extension orthosis use after treatment of Dupuytren contracture with needle aponeurotomy, although in a smaller patient population and with shorter duration of follow-up. Tam and Chung retrospectively reviewed 53 patients treated with needle aponeurotomy. At an average of 48.9 days follow-up, they found no significant difference in the gains of PIP or MCP ROM between patients treated with or without night orthosis use.1

The majority of cords treated in our study primarily affected the MCP joint (90%), with only 10% of cords affecting the PIP. All 3 patients with cords primarily affecting the PIP joint were in the orthosis group. This was reflected by a statistically significant greater PIP joint contracture in the orthosis group at baseline. The
lack of patients in the no orthosis group in addition to the low overall number of patients with primary PIP joint contractures in our study prevented meaningful conclusions of the effect of orthosis fabrication versus no orthosis fabrication after treatment with CCH in patients with primarily PIP joint contractures. However, several patients in each group with primarily MCP joint contractures also had concomitant contractures of the PIP joint that were not specifically treated.

There are several possible reasons for our observation that night extension orthosis use in addition to therapy did not provide benefit to TAE compared to hand therapy alone. Cyr and Ross suggested that early controlled motion was necessary to preserve the viscoelastic properties of connective tissue, especially with trauma and edema. Citron and Hearnden hypothesized that prolonged tension led to microruptures in the remaining fascia and induced hypertrophic scarring leading to recurrence of contracture.

It is also possible that we did not observe a benefit to TAE from night time orthosis use after the treatment of Dupuytren contracture with CCH because of errors in our orthosis fabrication technique. It is possible that orthosis fabrication to hold the treated finger in maximal comfortable extension resulted in excess tension on the wound that was detrimental to, or at least not beneficial to, ROM after treatment. In a retrospective series of 268 patients treated with surgical fasciectomy for Dupuytren contracture, Evans et al. treated patients after surgery with either a volar orthosis, with tension applied to hold the treated finger in near full extension, or a dorsal blocking orthosis, which blocked tension on the palmar fascia but allowed flexion exercises. They found that patients in the dorsal blocking group (no tension applied) had superior ROM and decreased scar formation. It is also possible that the duration of orthosis use in our study was not long enough to demonstrate benefit. Several studies have demonstrated that orthosis use improves the passive ROM of contracted PIP joints in a dose-dependent manner, with longer durations of orthosis use required to improve extension as opposed to flexion.

Our study has several limitations. This was a single-center study with a homogenous study patient population, which can limit the generalizability of our findings. The study was nonblinded; the patient and physician were aware of the treatment group. Furthermore, the primary investigator or his designee performed the assessments after the treatment, which could have allowed for the introduction of bias. Our study population of patients with primarily MCP joint contractures cannot be extrapolated to those with primarily PIP joint contractures. Our power analysis was based on the SD of trials examining treatment of Dupuytren contracture after fasciectomy, as there were no prior studies available on night time orthosis use after treatment with CCH. This study was also powered as a noninferiority trial on the effect of night time orthosis use after CCH treatment. This study was also powered as a noninferiority trial on the effect of night time orthosis use after treatment with CCH. The duration of orthosis use in this study was limited to 3 months at night, but the Food and Drug Administration recommendation for orthosis use after CCH treatment is 4 months. It is possible that after another month of orthosis use a benefit to TAE would have emerged. Nevertheless, the duration of night orthosis use in our study was the same as that of the prior RCTs on orthosis use after fasciectomy. Additionally, a longer duration of follow-up after the conclusion of orthosis use may have yielded different results. Of the prior RCTs on orthosis use after open fasciectomy, the trial by Collins et al. reported 3-month outcomes, and the studies by Jerosch-Herold et al. and Kemler et al. reported 3-month and 1-year outcomes, respectively. In all of these studies, no significant differences emerged with increased follow-up. The validity of our findings on the effect of orthosis use is limited by the compliance of patients in the orthosis group with their assigned treatment. By the completion of the 90-day follow-up, only 50% of the patients in the orthosis group reported that they had worn the orthosis every night as prescribed. The rate of orthosis compliance in our study was similar to that in the prior RCT assessing orthosis

### Table 4

| Response, n (%) | Orthosis Group (n = 12) | No Orthosis Group (n = 14) | P Value |
|----------------|------------------------|---------------------------|---------|
| Very satisfied | 6 (50%)                | 11 (79%)                  | .41     |
| Satisfied      | 4 (33%)                | 2 (14%)                   |         |
| Neutral        | 2 (17%)                | 1 (7%)                    |         |
| Dissatisfied   | 0 (0%)                 | 0 (0%)                    |         |
| Very dissatisfied | 0 (0%)               | 0 (0%)                   |         |

### Table 5

| Clinical Success, n (%) | Orthosis Group (n = 12) | No Orthosis Group (n = 14) | P Value |
|-------------------------|------------------------|---------------------------|---------|
| Successful              | 9 (75%)                | 13 (93%)                  | .31     |
| Not successful          | 3 (25%)                | 1 (7%)                    |         |

Figure 2. Graph showing the median TAE in each group, with ranges from the 25th to the 75th percentile.
use after fasciectomy. In our study, 67% of the patients wore the orthosis more than 50% of the time assigned compared with 75% of patients in the study by Jerosch-Herold et al. The conclusions above are based on an intention to treat analysis. The compliance in our study was high (93%) at initial follow-up and decreased over time. While it is possible that increased orthosis compliance would have resulted in the TAE benefit for the orthosis group, our results may represent the pragmatic reality of patient compliance with treatment over a prolonged period of time.

Similar to the findings of previous studies examining the effect of night orthosis use after the treatment of Dupuytren contracture with fasciectomy and needle aponeurotomy, our study of patients with primarily MCP joint contractures with a night extension orthosis after treatment with injectable CCH did not show improvement in TAE compared with hand exercises alone. Future studies will be required to critically assess the role of night orthosis use in larger, more heterogenous populations at longer time points; nevertheless, the present study calls in to question the short-term benefit of night time orthosis use following CCH treatment.

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