Dupuytren contracture is a benign fibroproliferative disorder of palmar fascia leading to flexion deformity of the fingers. Surgery continues to be the preferred treatment for significant disease; however, it does not provide a definitive cure, has high recurrence rates, and carries significant risk of complications.1,2 Over the last century, many nonsurgical options have been explored and failed to demonstrate clinical efficacy, including physical therapy; topical vitamin A and E; radiotherapy; and corticosteroid, prostaglandin E, and gamma interferon injections.3,4

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Clostridium histolyticum collagenase was first introduced as an injectable treatment for Dupuytren contractures nearly 2 decades ago. Since that time, several phase III clinical trials have demonstrated a significant advantage over placebo for the treatment of metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joint contractures, and collagenase injection has emerged as the only Food and Drug Administration–approved nonoperative modality.2-5

At the Veterans Association (VA) Medical Center, Tex., enzymatic fasciotomy via collagenase has provided 2 important benefits for our hand surgery population. First, more Dupuytren patients are candidates for treatment without the strict requirements for surgical clearance and the need for prolonged recovery. Second, we have more operating room availability, such that non-Dupuytren patients can be scheduled sooner for their elective surgery. The end result is that more patients are treated over a given time period.

To maximize this benefit for our patients, we modified our treatment protocol with the goal of minimizing the total time needed to achieve therapeutic success per joint contracture. Our early experience with collagenase treatment suggested that the most important rate-limiting factors were (1) the number of injections needed for successful treatment and (2) the availability of surgeon for cord manipulation. If the contracture is not corrected after the first injection, patients wait 30 days before undergoing another injection for up to 3 injections per joint. If the surgeon is required for cord manipulation and clinic day is consistently followed by a full operative day (as is the case at our institution), the number of patients who can be treated is limited by the time the surgeon has to perform manipulation between cases.

METHODS

This study was approved by the VA Medical Center Institutional Review Board.

All patients at the VA Medical Center treated with injectable collagenase for Dupuytren contracture using our hand therapist-based protocol from 2011 to 2013 were included in the study. Treatment consisted of the manufacturer-recommended dose (0.58 mg) of collagenase clostridium histolyticum (Xiaflex; Auxilium Pharmaceuticals, Inc, Malvern, Pa.) spread over 3 injections, several millimeters apart, and injected directly into the cord affecting the joint. Patients returned to the clinic 24 hours after injection. At that time, they received a digital block from a physician assistant (PA) with a 50:50 mixture of 0.25% bupivacaine:1% lidocaine and subsequently underwent cord manipulation by a certified hand therapist (CHT). After cord manipulation, the CHT and the PA assessed the digit for signs of vascular compromise, integrity of flexor digitorum superficialis and profundus tendons, and skin tear. Skin tears were dressed with a compressive dry dressing. With the exception of skin tears, the CHT and the PA were instructed to contact in-house hand surgeon for immediate evaluation if there was any concern that the patient had experienced a serious adverse event.

Occupational Therapy Specific Protocol

The patient’s forearm is placed in neutral with the wrist in full flexion to decrease the chances of flexor tendon rupture. The MCP joint of the affected digit is fully flexed. While maintaining full passive wrist and MCP flexion, the PIP and distal interphalangeal joint is brought slowly into maximum extension. Then the MCP extension is added until the digit is in maximum extension. Typically, the cord will release at this point. To address any residual cord the patient-controlled wrist extension is added with the palm flat on the table while asking the patient to raise their elbow until the wrist is extended to maintain the stretch for 15-20 seconds. To target palmar pitting, the palmar spreading technique can be performed by taking the patient’s hand and spreading the thenar and hypothenar eminences apart. Lastly, the affected and adjacent digits can be extended into oblique stretches to further release any remaining cords. After cord rupture, the CHT fabricated a hand-based static splint to keep digit in maximum extension, and patients were instructed on blocking, reverse blocking, and tendon-gliding exercises. The splint is worn at all times when not performing exercises for the first week and in night thereafter for 6 months. Patients were asked to return to follow-up with the hand surgeon at a minimum of 1 week, 1 month, and 6 months after manipulation.

Treatment success was defined as the reduction of flexion contracture to 5 degrees or less after cord rupture. Recurrence was defined as return to >10 degrees of contracture in successfully treated joints. Additionally, we recorded whether or not skin tears occurred during cord manipulation. Charts were also reviewed for the evidence of major treatment-related adverse events, including injection site infection, wound (skin tear) infection, injury to flexor tendon and/or pulley, neurovascular injury, ligamentous injury, finger deformity, complex regional pain syndrome, and any condition requiring additional medical/surgical treatment or hospitalization.

Data for each treated joint were organized in a spreadsheet (Excel; Microsoft Corp., Redmond, Wash.). Means were calculated to summarize the categorical data. Chi-squared analysis was used to compare outcomes between MCP and PIP joints,
between fingers with and without tears, and between our study and previous phase III trials. A 2-sample t-test analysis was used to compare the preinjection contracture severity between successfully treated joints and those that failed treatment and between joints with skin tears and those without. A value of $P < 0.05$ was considered significant. Analyses were performed using the Excel spreadsheet software.

**RESULTS**

Between 2009 and 2012, 36 patients (47 joints) were treated for Dupuytren contractures with injectable collagenase using our occupational therapy-based protocol. Thirty-three men and 3 women had a mean age of 65.1 years (range, 47–80 years). The mean contracture was 47.5 degrees. There were 40 MCP joint contractures ranging from 20 to 85 degrees (mean, 46.7 degrees) and 7 PIP joint contractures ranging from 30 to 70 degrees (mean, 52.1 degrees) that underwent treatment. One joint was treated per patient encounter, and each joint received a single injection. None of the patients underwent multiple injections of the same joint.

Thirty-six of the 47 joints (76.6%) had contractures reduced to 5 degrees or less after cord manipulation. The preinjection contractures in joints that failed to be reduced to 5 degrees or less (mean, 64.1 degrees; range, 30–85 degrees) were significantly greater than in those treated successfully (mean, 42.8 degrees; range, 25–70 degrees; $P = 0.013$). The treatment success rate did not differ significantly between MCP and PIP joints (80.0% and 57.1%, respectively; $P = 0.18$). Thirty-day follow-up information was available for 32 of the 36 successfully treated joints (29 MCP, 3 PIP). Two joints (6.7%) had recurrence of contracture to >10 degrees. Although both recurrences occurred in MCP joints, the difference in recurrence rates between MCP and PIP joints did not reach statistical significance (6.9% and 0%, respectively; $P = 0.64$).

Skin tears occurred in 18 of the 47 joint manipulations (38.3%). The preinjection contractures in those with skin tears (mean, 55.0 degrees; range, 20–85 degrees) were significantly greater than that in those without skin tears (mean, 42.8 degrees; range, 25–70 degrees; $P = 0.057$). All skin tears healed by secondary intention without complication using basic local wound care (wash twice daily with soap and water, pat dry, and apply triple antibiotic ointment and bandage). None of the patients experienced any major treatment-related adverse events.

**DISCUSSION**

This retrospective chart review supports the efficacy of our protocol for injectable collagenase treatment of Dupuytren contracture. Table 1 displays the results of this study and the results of the 3 double-blind placebo-controlled phase III clinical trials that were presented in the briefing document for injectable collagenase submitted to the Food and Drug Administration in 2009, which included the Collagenase Option for the Reduction of Dupuytren’s Cord (CORD I) and CORD II studies. In these studies, joints could receive additional injections if contracture was not reduced to $\leq 5$ degrees 30 days after the previous injection for a maximum of 3 injections per joint. Between all 3 studies, 29% of joints received

|                       | CHT-Based Protocol | CORD I/AUX-CC-857 | CORD II/AUX-CC-859 | DUPY-303 |
|-----------------------|--------------------|-------------------|--------------------|----------|
| Total joints          | 47                 | 203               | 45                 | 23       |
| Achieving reduction in contracture to $\leq 5$ degree, % (number) | 76.6 (36)          | 64.0 (130)        | 44.0 (20) | 91.3 (21) |
| Mean number of injections per joint | 1.0                | 1.5               | 1.5                | 1.4      |
| Preinjection contracture, degree | 47.5              | 50.2              | 53.2               | 52.0     |
| MCP joints            | 40                 | 133               | 20                 | 14       |
| Achieving reduction in contracture to $\leq 5$ degree, % (number) | 80.0 (32)          | 76.7 (102)        | 65.0 (13) | 85.7 (12) |
| Mean number of injections per joint | 1.0                | 1.6               | 1.4                | 1.3      |
| Preinjection contracture, degree | 46.7              | 48.0              | 49.5               | 53.2     |
| PIP joints            | 6.0                | 7.2               | 7.5                | 3.6      |
| Achieving reduction in contracture to $\leq 5$ degree, % (number) | 57.1 (4)           | 40.0 (28)         | 28.0 (7)  | 100 (9) |
| Mean number of injections per joint | 1.0                | 1.3               | 1.7                | 1.6      |
| Preinjection contracture, degree | 52.1              | 54.4              | 56.2               | 50.0     |
| Contracture after last injection, degree | 14.3              | 21.7              | 24                 | 0        |
1 injection, 22% received 2, and 49% received 3 (Fig. 1). We compared the results of our protocol with those of each phase III clinical trial. Aside from having a higher success rate for all joints versus the CORD II study (76.6% versus 44.0%; \( P = 0.0016 \)) and a lower success rate for PIP joints when compared with the DUPY-303 study (57.1% versus 100%; \( P = 0.029 \)), our protocol achieved outcomes compa-
rable ($P > 0.05$) with these 3 studies, despite utilizing only a single injection for all joints (Figs. 2 and 3).

The CORD I$^6$ and CORD II$^7$ studies described a “standard manipulation technique” in which patients returned 24 hours after injection, and the surgeon performed passive extension with sustained pressure to the extent of patient pain tolerance. Persistent tension was kept on the cord for 10–20 seconds per attempt for up to 3 attempts with 5–10 minutes between each attempt. If the contracture was not reduced to 5 degrees or less, patients could elect to have another injection 30 days later. The majority of patients underwent multiple injections before completing treatment. In our study, therapists were able to perform their manipulations without strict time or attempt limitations. Moreover, digital block ensured that the level of force applied to induce cord rupture was determined by the therapist and not by patient pain tolerance. This likely contributed to the high rate of successful contracture release after a single treatment, with the trade-off being a higher rate of skin tears.

According to the combined results of 13 clinical trials (1082 patients), adverse events occurred in 98% of patients receiving injectable collagenase.$^2$ The most common treatment-related adverse events, each occurring in at least one-third of patients, were peripheral edema, contusion, injection site pain/hemorrhage, and pain in the extremity. Major treatment-related adverse events were rare: 3 flexor tendon ruptures, 1 pulley rupture with ligament injury, and 1 Boutonniere deformity. Skin tears, a complication that occurs during cord manipulation, were experienced in 12.7% of clinical trial patients.$^2$ Although not considered a serious adverse event, skin tears can be painful and result in an open wound, both of which can be distressing for the patient.$^9,10$ Skin tears occurred in 38.3% of patients in our study. We believe that the ability to achieve cord rupture with a single injection outweighs the potential downsides of a skin tear, as these wounds tend to heal without complication with basic wound care. Contrary to other reports in the literature,$^9,10$ we have found our patients to be very accepting of skin tears as a relatively frequent complication of treatment. Another factor that could have effected the higher rate of success is the therapist’s assisted extended stretch of the cord using the “patient controlled wrist extension,” which likely resulted in the a larger skin tear as well. Ordinarily, despite seemingly achieving full extension during manipulation, directly visualizing the start of a larger skin tear may discourage the manipulator to continue extension. With palm flat on the table and “patient controlled wrist extension” maneuver, the skin tear is not readily visualized and will not scare the manipulator into terminating the extension prematurely, resulting in rupture of the residual cord and potentially better long-term outcome.

The results of our initial experience with the CHT-based protocol support its continued use in our institution. It is possible a higher percentage of joints in our study would have attained treatment.
success had they received additional treatments. At this time, we have not treated a single cord with more than 1 injection. Patients with contractures that were not reduced to 5 degrees or less were either lost to follow-up or satisfied with the outcome achieved after a single injection.

Although these initial results are encouraging, relatively few joints (47) have been treated using the CHT-based protocol, and even fewer were available for evaluation at 30-day and 6-month follow-ups. Although it is unlikely that the recurrence rate would be affected by who performs successful cord rupture, future studies would benefit from larger numbers of treated joints and long-term follow-up data for each. In addition, it would be beneficial to identify additional patient risk factors that predispose to skin tears, such as contracture duration before treatment. This could allow for more accurate counseling regarding the likelihood of this complication.

CONCLUSIONS

Injectable collagenase provides an attractive office-based treatment alternative for patients with significant Dupuytren contracture wishing to avoid the risk, process, and prolonged recovery associated with surgery. Our CHT-based protocol offers the benefits of high single treatment success rate and decreased surgeon time requirement. Patients should be counseled on the risk of skin tears, which is higher for those with more severe contractures.

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