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Original Research

Collagenase Clostridium Histolyticum for the Treatment of Dupuytren Disease: A Delphi-Based Consensus Study

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Purpose: The aim of this study was to establish the consensus recommendations among hand surgeons who were experts in the use of collagenase clostridium histolyticum (CCH) on the appropriate treatment of Dupuytren disease in well-defined patient populations with varying degrees of disease severity and functional impairment.
Methods: A three-round, blinded, modified Delphi process examined panelists' approaches to CCH treatment of metacarpophalangeal (MP) or proximal interphalangeal (PIP) joint contractures involving one or two fingers with varying degrees of severity. Clinical scenarios related to poor-quality skin, postfasciectomy scarring, boutonnière deformity, closed capsulotomy, and blood thinner use were also presented for panelist consideration. Panelists provided responses to clinical scenarios using a 5-point Likert scale or a yes/no response. Consensus was defined as ≥66.7% panelist agreement or disagreement.
Results: Twenty panelists completed round 1; 19 of the 20 panelists completed rounds 2 and 3. Panelists achieved a high level of consensus for using CCH for the treatment of patients with palpable cords and varying severity contractures representing one- or two-finger MP joint contractures, most one- or two-finger PIP joint contractures, and most combined MP and PIP joint contractures. Consensus for the treatment of PIP joint contractures was mostly achieved, but clinical scenarios related to recurrent PIP contracture with poor-quality skin and/or significant postfasciectomy scarring, boutonnière deformity, PIP contractures >70°, closed capsulotomy, and blood thinner use were modified, and then most (95.3%) statements reached consensus for agreement in round 2. In round 3, open-ended responses indicated that panelists considered CCH appropriate for most patients with Dupuytren disease.
Conclusions: Consensus-based findings among expert hand surgeons with substantial CCH experience indicated that CCH has a wide-ranging application for the treatment of Dupuytren disease in patients with varying degrees of disease severity and functional impairment.
Type of study/level of evidence: Therapeutic V.

Dupuytren disease (DD) is estimated to affect 8.2% of individuals globally. It is a heterogenous fibroproliferative condition of the palmar fascia that is characterized by the development of fascial nodules and cords, resulting in digital contracture affecting hand function.[1–3] The presence of a nodule on the hand often precedes the formation of a palmar cord and finger contracture.[4] The metacarpophalangeal (MP) joint, the proximal interphalangeal (PIP) joint, or both joints are affected in DD.[4] One hand is usually affected first, with some patients experiencing DD in both hands.[4] Patients with symptomatic DD typically present with fixed flexion deformities, restricted range of motion, and functional impairments that affect activities of daily living.[4–6] Treatment options include both nonsurgical (eg, collagenase clostridium histolyticum [CCH] injection [Xiaflex, Endo Pharmaceuticals Inc]) and surgical interventions (eg, dermofasciectomy,

Declaration of interests: G.M.P. reports serving on the speakers' bureau for Endo Pharmaceuticals Inc. and receiving royalties from Zimmer-Biomet for the trigger release knife. D.H. is an employee of Endo Pharmaceuticals Inc. J.R.V. reports serving on the speakers' bureau for Endo Pharmaceuticals Inc. P.B. reports serving on the speakers' bureau for Axogen and Endo Pharmaceuticals Inc.; and owning stock in Cytori.

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fasciectomy, needle aponeurotomy, dynamic external fixation, or percutaneous needle fasciotomy).[1,7] Less common surgical approaches include PIP joint arthrodesis in a subset of revision cases and even possible amputation for particularly severe recurrences.

CCH injection, approved by the US Food and Drug Administration for the treatment of DD in 2010, is indicated for the treatment of adults with Dupuytren contracture with a palpable cord.[8] Clinical trial data[9–11] and a systematic literature review[12] support the efficacy of CCH for the treatment of DD. Phase 3 trials showed the efficacy of injectable CCH for decreasing single finger, ≤2-joint contractures of the MP or PIP joints of ≥20°, and improving range of motion in patients with DD,[9–11] including 1-year durability of response.[11] A post hoc analysis of data from one of the phase 3 trials[9] showed that injectable CCH was effective in improving contracture for patients with varying severities of DD.[13]

A survey was developed using a modified Delphi process to identify areas of agreement among experienced hand surgeons with CCH expertise, based on responses to questions related to the use of CCH in well-defined patient populations (eg, MP or PIP contracture) with varying degrees of disease severity and functional impairment (eg, single or multiple fingers affected). The Delphi process is an established, proven method to gain consensus from a panel of experts on a specific topic of interest.[14] The aim of the current Delphi approach was to assess hand surgeon consensus on the use of CCH for various clinical scenarios for the treatment of DD and obtain valuable insights into the real-world applications of CCH from experienced users.

Materials and Methods

The modified Delphi survey process consisted of three blinded online rounds of questioning. A steering committee was established in collaboration with Endo Pharmaceuticals. This steering committee developed the protocol for iteratively gathering insights into the appropriate, real-world use of CCH for treating patient populations with DD of varying degrees of disease severity and functional impairment. The steering committee identified hand surgeons, and only those who had substantial experience with CCH treatment for DD were invited to participate as panelists. Each round of questioning was completed independently and anonymously online by each panelist. Round 1 was launched on January 19, 2021, round 2 on May 4, 2021, and round 3 on September 14, 2021. This article does not contain any studies with human or animal subjects.

Survey rounds

Panelists were presented 22 real-world case scenarios and, for each scenario, provided statements for the administration of CCH to treat MP and/or PIP joint contractures involving one finger or two fingers, with varying degrees of contracture and clinical severity (Fig. 1). Each scenario presented a distinct contracture(s) with a series of statements to evaluate the impact of patient- or disease-related features (ie, patient age, disease recurrence, medical risk with the use of anesthesia, Dupuytren diathesis, poor-quality skin, and postfasciectomy scarring) on the clinical decision to treat with CCH. Treatment of thumb contractures and closed capsulotomy and the use of CCH in patients taking blood thinners other than aspirin were also explored.

For round 1, panelists selected either a yes/no response or rated the information on a 5-point Likert scale (1 [“strongly disagree”], 2 [“disagree”], 3 [“deficient information”], 4 [“agree”], and 5 [“strongly agree”]) depending on the scenario and statement presented. Panelists’ level of agreement for each statement was determined, with a consensus threshold of ≥66.7% for agreement (“strongly agree” and “agree”) or disagreement (“strongly disagree” and “disagree”). After completion of round 1, the responses were analyzed, consensus statements were identified, and the feedback provided by the panelists was used by the steering committee to modify the statements that lacked consensus for inclusion in round 2.

As noted above, statements that did not meet the ≥66.7% threshold for consensus in round 1 were reassessed in round 2. In addition, scenarios exploring the “impact of patient decision” (eg, patient declines open surgical procedure) on various clinical scenarios were recommended for inclusion by the steering committee during this round. Statements were rated as described for round 1. Statements failing to reach consensus in round 2 were reassessed in round 3. Also, for round 3, based on recommendations from the steering committee and feedback from panelists, the clinical decision-making process was explored using an open-ended response methodology.

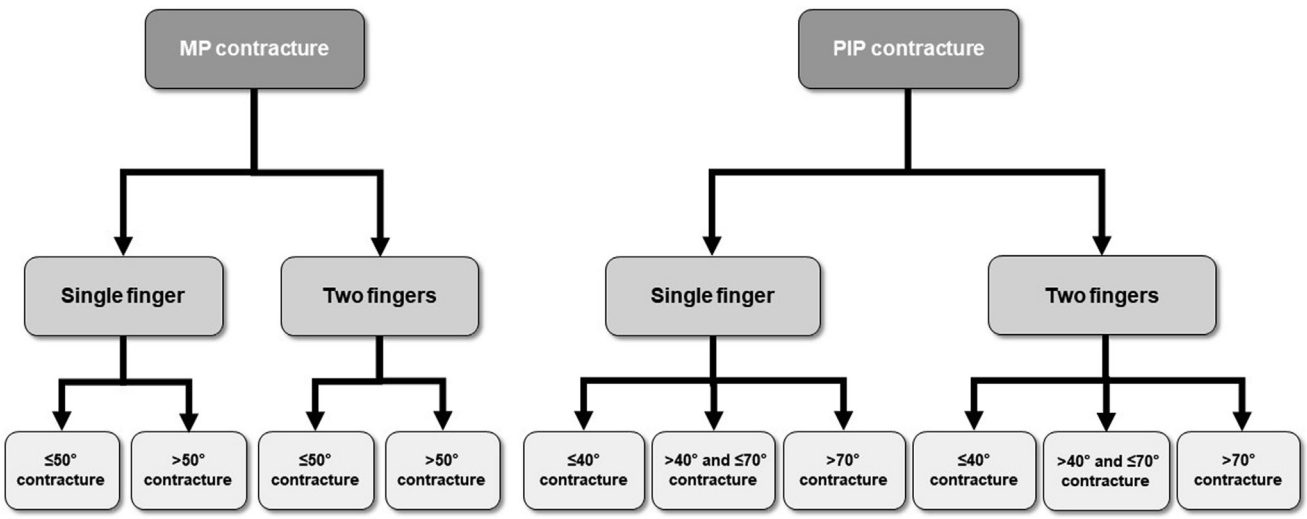


Figure 1. Overview of clinical scenarios examined for MP and PIP contractures alone and in combination.

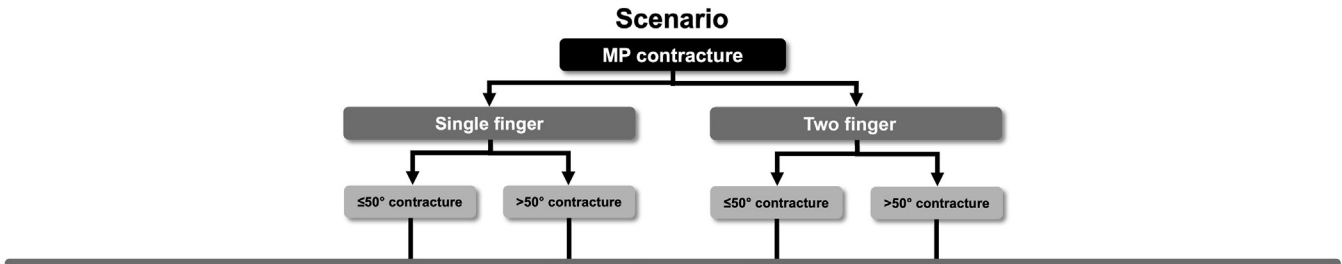
Table 1
Demographic Characteristics of the Expert Panel

Parameter, *n*	Panelists (*N* = 20)
Experience practicing medicine postresidency/training	
5–9 y	1
10–14 y	3
15–19 y	3
≥20 y	13
Practice setting	
Group—single specialty	11
Group—multispecialty	5
Individual	1
Academic	3
Board certification	
Hand surgery	18
Orthopedic surgery	16
Plastic surgery	3
General surgery	1
Completion of hand surgery fellowship	20
Number of patients with DD treated with open surgery during the past year	
0	3
1–10	8
11–24	4
25–49	2
≥50	3
Years using CCH as treatment for DD	
6–9 y	5
≥10 y	15
Number of patients with DD treated with CCH during past year	
11–24	5
25–49	7
≥50	8
Formal training in use of CCH during fellowship	
Yes	3
No	2
Trained before approval	15

Results

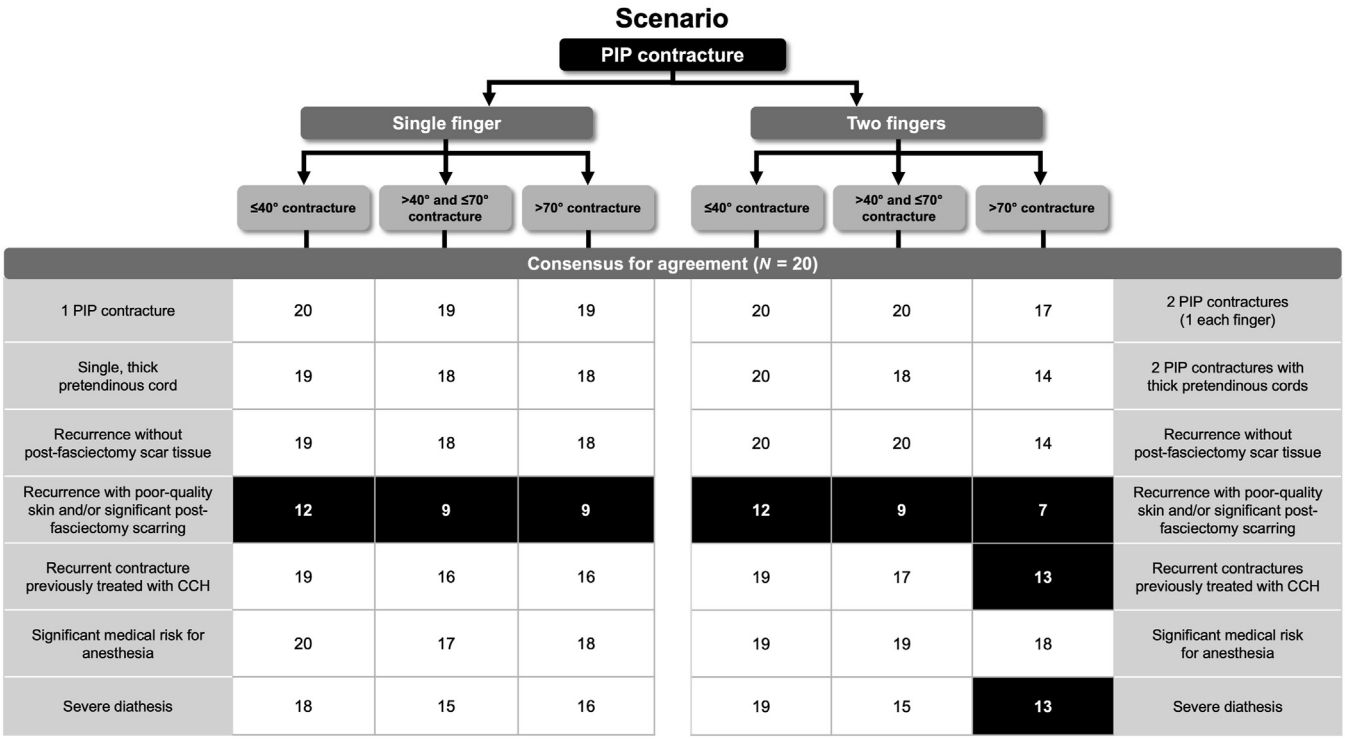
Twenty hand surgeons with substantial CCH experience (all reported ≥6 years of CCH experience, and 40.0% treated ≥50 patients with DD with CCH during the previous year [Table 1]) completed round 1, and 19 completed rounds 2 and 3. In round 1, 163 of the 190 statements (85.8%) concerning 22 scenarios related to the palpable cord(s) with MP (Fig. 2) or PIP joint contractures (Fig. 3) reached agreement consensus. Regarding scenarios related to combinations of MP and PIP joint contractures, most reached an agreement consensus, with the exception of the scenario related to recurrence with poor-quality skin and/or significant postfasciectomy scarring (Fig. 4).

In round 1, for 18 scenarios describing PIP contractures alone or with MP contractures, 17.3% of statements did not achieve agreement consensus (eg, poor-quality skin and postfasciectomy scarring; Table 2). All scenarios regarding CCH treatment for patients with thumb MP and/or interphalangeal contracture achieved agreement consensus (Table 3). In round 2, most statements (95.3%) reached an agreement consensus for CCH use; none reached a disagreement consensus. Scenarios describing PIP contractures associated with "poor-quality skin," "scarring," and "boutonnière deformity" not achieving consensus during round 1 (Table 2) were revised for round 2 to include additional context for clarity, with most scenarios achieving 100% agreement consensus (Table 4). All round 2 statements on the impact of patient decisions achieved agreement consensus. The two round 1 scenarios related to "two fingers, each with a PIP joint contracture >70° and no boutonnière deformity" that were reassessed in round 2 without modification for clarity had agreement consensus for CCH use: 2 recurrent PIP contractures >70° previously treated with CCH and 2 PIP contractures >70° and severe Dupuytren diathesis.



Consensus for agreement (*N* = 20)					
1 MP contracture	19	19	19	19	2 MP contractures (1 each finger)
Single, thick pretendinous cord	19	20	20	20	2 MP contractures with thick pretendinous cords
Recurrence without post-fasciectomy scar tissue	20	20	19	20	Recurrence without post-fasciectomy scar tissue
Recurrence with poor-quality skin and/or significant post-fasciectomy scarring	15	15	15	15	Recurrence with poor-quality skin and/or significant post-fasciectomy scarring
Recurrent contracture previously treated with CCH	20	20	19	19	Recurrent contractures previously treated with CCH
Significant medical risk for anesthesia	20	20	20	19	Significant medical risk for anesthesia
Severe diathesis	19	19	19	19	Severe diathesis

Figure 2. Clinical scenarios with consensus for agreement for treatment of MP joint contracture with CCH.



1 PIP contracture	20	19	19	20	20	17	2 PIP contractures (1 each finger)
Single, thick pretendinous cord	19	18	18	20	18	14	2 PIP contractures with thick pretendinous cords
Recurrence without post-fasciectomy scar tissue	19	18	18	20	20	14	Recurrence without post-fasciectomy scar tissue
Recurrence with poor-quality skin and/or significant post-fasciectomy scarring	**12**	**9**	**9**	**12**	**9**	**7**	Recurrence with poor-quality skin and/or significant post-fasciectomy scarring
Recurrent contracture previously treated with CCH	19	16	16	19	17	**13**	Recurrent contractures previously treated with CCH
Significant medical risk for anesthesia	20	17	18	19	19	18	Significant medical risk for anesthesia
Severe diathesis	18	15	16	19	15	**13**	Severe diathesis

Figure 3. Clinical scenarios with consensus for agreement for treatment of PIP joint contracture with CCH. Scenarios with results not meeting consensus for agreement are shaded black.

Scenarios pertaining to closed capsulotomy were evaluated, with one of the two scenarios achieving agreement consensus in round 1 (80%; Table 5). The second scenario was modified for clarity and reassessed in round 2, and one of the two modified scenarios achieved agreement consensus (68.4%; Table 5). In round 1, consensus was achieved for scenarios related to patients with DD receiving nonaspirin blood thinner (ie, warfarin, clopidogrel, novel oral anticoagulants [eg, apixaban and rivaroxaban]) that require 1 vial of CCH (Table 6). The same scenario requiring two vials did not reach agreement consensus in round 1 (60%), but all panelists who agreed in round 1 were in agreement, regardless of the blood thinner used. In round 2, the same scenario requiring two vials achieved agreement consensus (89.5%) without modification. Regarding remaining CCH in a vial after a procedure, 50.0% (round 1) and 57.9% (round 2)

Scenario (*N* = 20)

	Single finger, *n*						Two fingers, *n*					
MP contracture (degrees)	≤50°			>50°			≤50°			>50°		
PIP contracture (degrees)	≤40°	>40° and ≤70°	>70°	≤40°	>40° and ≤70°	>70°	≤40°	>40° and ≤70°	>70°	≤40°	>40° and ≤70°	>70°
1 finger with MP contracture and PIP contracture	20	20	18	20	20	19						
Two fingers, one with MP contracture and the other with PIP contracture							20	20	20	20	19	20
Contractures with thick cords	**19**	**19**	**16**	**20**	**18**	**18**	**20**	**19**	**17**	**20**	**17**	**18**
Recurrence without post-fasciectomy scar tissue	**19**	**18**	**17**	**20**	**18**	**17**	**20**	**17**	**18**	**19**	**17**	**16**
Recurrence with poor-quality skin and/or significant post-fasciectomy scarring	**13**	**10**	**9**	**12**	**9**	**8**	**14**	**12**	**9**	**12**	**10**	**8**
Recurrent contractures previously treated with CCH	**19**	**18**	**15**	**19**	**18**	**15**	**19**	**16**	**17**	**19**	**15**	**16**
Significant medical risk for anesthesia	**19**	**19**	**18**	**19**	**17**	**18**	**19**	**18**	**19**	**18**	**18**	**18**
Severe diathesis	**18**	**16**	**15**	**18**	**15**	**15**	**17**	**17**	**15**	**17**	**15**	**14**

Figure 4. Clinical scenarios with consensus for agreement for CCH treatment of MP and PIP joint contractures affecting a single, or both, fingers. Scenarios with results not meeting consensus for agreement are shaded black.

Table 2
Clinical Scenarios Describing PIP Contractures Either Alone or With MP Contractures That Did Not Achieve Consensus* in Round 1 ($N = 20$)

Clinical Scenario†	Agreement, *n*
One finger with PIP joint contracture alone and no boutonnière deformity	
One recurrent PIP contracture ≤40°	
With poor-quality skin and/or significant postfasciectomy scarring	12
One recurrent PIP contracture >40° and ≤70°	
With poor-quality skin and/or significant postfasciectomy scarring	9
One recurrent PIP contracture >70°	
With poor-quality skin and/or significant postfasciectomy scarring	9
Two fingers, each with a PIP joint contracture and no boutonnière deformity	
Two recurrent PIP contractures ≤40°	
With poor-quality skin and/or significant postfasciectomy scarring	12
Two fingers, each with a PIP contracture >40° and ≤70°	
Would your clinical judgment change if this patient had a boutonnière deformity? No	13
Two recurrent PIP contractures with poor-quality skin and/or significant postfasciectomy scarring	9
Two fingers, each with a PIP contracture >70°	
Would your clinical judgment change if this patient had a boutonnière deformity? No	13
Two recurrent PIP contractures with poor-quality skin and/or significant postfasciectomy scarring	7
Two recurrent PIP contractures previously treated with CCH	13
Two PIP contractures and severe diathesis	13
One finger with an MP joint contracture and a PIP contracture and no boutonnière deformity	
One finger with a recurrent MP contracture ≤50° and a PIP contracture ≤40°	
With poor-quality skin and/or significant postfasciectomy scarring	13
One finger with an MP contracture ≤50° and a PIP contracture >40° and ≤70°	
Would your clinical judgment change if this patient had a boutonnière deformity? No	13
One recurrent MP contracture and a PIP contracture with poor-quality skin and/or significant postfasciectomy scarring	10
One finger with a recurrent MP contracture ≤50° and a PIP contracture >70°	
With poor-quality skin and/or significant postfasciectomy scarring	9
One finger with a recurrent MP contracture >50° and a PIP contracture ≤40°	
With poor-quality skin and/or significant postfasciectomy scarring	12
One finger with an MP contracture >50° and a PIP contracture >40° and ≤70°	
Would your clinical judgment change if this patient had a boutonnière deformity? No	12
One recurrent MP contracture and a PIP contracture with poor-quality skin and/or significant postfasciectomy scarring	9
One finger with an MP contracture >50° and a PIP contracture >70°	
Would your clinical judgment change if this patient had a boutonnière deformity? No	12
One recurrent MP contracture and a PIP contracture with poor-quality skin and/or significant postfasciectomy scarring	8
Two fingers, one with an MP joint contracture and the other with a PIP contracture and no boutonnière deformity	
Two fingers, one with an MP contracture ≤50° and the other with a PIP contracture >40° and ≤70°	
Would your clinical judgment change if this patient had a boutonnière deformity? No	13
Both with recurrent contractures and both with poor-quality skin and/or significant postfasciectomy scarring	12
Two fingers, one with an MP contracture ≤50° and the other with a PIP contracture >70°	
Would your clinical judgment change if this patient had a boutonnière deformity? No	12
Both with recurrent contractures and both with poor-quality skin and/or significant postfasciectomy scarring	9
Two fingers, one with a recurrent MP contracture >50° and the other with a recurrent PIP contracture ≤40°	
Both with poor-quality skin and/or significant postfasciectomy scarring	12
Two fingers, one with a recurrent MP contracture >50° and the other with a recurrent PIP contracture >40° and ≤70°	
Both with poor-quality skin and/or significant postfasciectomy scarring	10
Two fingers, one with an MP contracture >50° and the other with a PIP contracture >70°	
Would your clinical judgment change if this patient had a boutonnière deformity? No	12
Both with recurrent contractures and both with poor-quality skin and/or significant postfasciectomy scarring	8

* Consensus was defined as ≥66.7% agreement ("strongly agree" and "agree") or disagreement ("strongly disagree" and "disagree") among respondents.
† Panelists were asked "Based on your clinical experience and current practice, CCH is an appropriate therapeutic intervention for patients with a palpable cord(s) who present with: [*insert clinical scenario*]."

of panelists would use remaining CCH to treat Garrod's nodules along the dorsal aspect of PIP joints.

During round 3, both statements related to poor-quality skin that were reassessed achieved agreement consensus: two fingers, each with a PIP joint contracture >70° and no boutonnière deformity (68.4%), and two fingers, one with an MP contracture ≤50° and the other with a PIP joint contracture >70° and no boutonnière deformity (79.0%). Panelists also openly described scenarios in which they would use CCH for DD; these included most or all MP joints or PIP joints (Table 7) and took patient preference into consideration.

Table 3
Clinical Scenarios Describing Thumb Contractures ($N = 20$)

Clinical Scenario	Agreement, *n*
Based on your clinical experience and current practice, CCH is an appropriate therapeutic intervention for patients with a palpable cord(s) who present with:	
An MP thumb contracture	20
An IP thumb contracture	17
MP and IP thumb contractures	17
First web space thumb contracture	19

Discussion

The rationale for this survey was to obtain information regarding real-world DD treatment with CCH from hand surgeons experienced with its use, given that presentation in clinical practice can vary widely. The consensus-based findings indicated that CCH treatment has wide-ranging applications for DD across a broad range of disease severity and functional impairment, beyond the limited indications typically reported in trials. These findings

Table 4
Summary of Modified Clinical Scenarios and Consensus Achieved (Round 2; $n = 19$)

Category	Clinical Scenario	Statements Reaching Consensus for Agreement (%)
Poor-quality skin	Based on your clinical experience and current practice, CCH is an appropriate therapeutic intervention for patients who present with recurrent PIP contracture(s) with poor-quality skin (ie, deficient skin) and *distinct* palpable cord(s).	
	Following the manipulation, the patient will develop *a minor skin tear with NO exposed tendon*.	100
	Following the manipulation, the patient will develop *a major skin tear with exposed tendon*.	88.2
Postfasciectomy scarring	Based on your clinical experience and current practice, CCH is an appropriate therapeutic intervention for patients who present with recurrent PIP contracture with significant postfasciectomy scarring and *distinct* palpable cord(s).	100
Boutonnière deformity	Would your clinical judgment for the use of CCH for the following contracture severities change if the patient had a boutonnière deformity that you would treat at the same time (eg, CCH and terminal extensor tenotomy under local anesthesia at the time of manipulation)?	100
Impact of patient decision	Based on your clinical experience and current practice, CCH is an appropriate therapeutic intervention for patients who present with the following contracture severities, and *in addition to the clinical findings, the patient does not want an open surgical procedure*.	100

Table 5
Closed Capsulotomy Scenarios ($N = 20$).

	Yes, *n* (%)	No, *n* (%)
Round 1		
Scenario 1.		
A patient presents with a 50° contracture of the PIP joint. After maximal flexion of the finger, you determine that 20° of that contracture is due to an independent PIP joint volar capsular contracture because you are able to de-tension the cord completely. Based on your clinical experience and current practice, is CCH combined with a closed capsulotomy of the PIP joint an appropriate therapeutic intervention for a patient whose capsular contracture has sufficient stretch to make it amenable to closed capsulotomy?	**16 (80)***	4 (20)
Scenario 2.		
If a patient initially presents with a contracture of 70° and, following CCH injection and manipulation, is left with a 20° contracture that you think is caused by a PIP joint volar capsular contracture, would you perform a closed capsulotomy?	10 (50)	10 (50)
Round 2		
Modification of Scenario 2 (from Round 1)		
If a patient initially presents with a contracture of 70° and, following CCH injection and manipulation, is left with a 20° contracture that you think is caused by a PIP joint volar capsular contracture that you think is readily amenable to closed capsulotomy, would you perform a closed capsulotomy?	**13 (68.4)**	6 (31.6)
Modification of Scenario 2 (from Round 1)		
A patient initially presents with a contracture of 70° and, following CCH injection and manipulation, is left with a 20° contracture that you think is caused by a PIP joint volar capsular contracture. Do you always attempt a closed capsulotomy if a patient is left with a 20° contracture after PIP joint manipulation?	8 (42.1)	11 (57.9)

* Bold indicates that consensus for agreement was achieved.

Table 6
Blood Thinner Scenarios ($N = 20$).

Clinical Scenario	Agreement, *n*
1 vial of enzyme	
Based on your clinical experience and current practice, CCH is an appropriate therapeutic intervention for patients with a palpable cord(s) who are on a blood thinner other than aspirin and who present with contractures that require 1 vial of enzyme	17
For those in agreement ($n = 17$)	
This clinical judgment would remain the same for patients who are receiving warfarin (Coumadin)	16
This clinical judgment would remain the same for patients who are receiving clopidogrel (Plavix)	17
This clinical judgment would remain the same for patients who are receiving a NOAC (eg, apixaban [Eliquis], rivaroxaban [Xarelto])	17
2 vials of enzyme	
Based on your clinical experience and current practice, CCH is an appropriate therapeutic intervention for patients with a palpable cord(s) who are on a blood thinner other than aspirin and who present with contractures that require 2 vials of enzyme	12
For those in agreement (n = 12)	
This clinical judgment would remain the same for patients who are receiving warfarin (Coumadin)	12
This clinical judgment would remain the same for patients who are receiving clopidogrel (Plavix)	12
This clinical judgment would remain the same for patients who are receiving a NOAC (eg, apixaban [Eliquis], rivaroxaban [Xarelto])	12

NOAC, novel oral anticoagulant.

provide insights into additional uses for CCH in patients with DD, including patients who take blood thinners. High-level consensus for agreement was achieved for using CCH for the treatment of MP joint contractures of varying severity and regardless of contracture severity ($\leq 50°$ or $>50°$), including patients with thumb MP alone and/or with thumb interphalangeal contractures. Statements related to "poor-quality skin," "scarring," "boutonnière deformity," and the use of CCH for treating PIP joint contractures of varying

Table 7
Clinical Scenarios Leading to the Use of CCH for Dupuytren-Related PIP Contractures as Described by Panelists

Respondent	Response*
1	I use CCH for all Dupuytren PIP joint contractures.
2	As long as the patient wants injection, we will do that first. Surgery can always be done.
3	I use CCH for an MP contracture >30° if there is a distinct palpable cord and the patient is functionally limited by the contracture. The same is true for a PIP contracture although I will consider CCH if the PIP contracture is <30° as long as there is a distinct cord and functional limitations. I favor CCH when the Dupuytren is primary or recurrent as I believe the risks are less with CCH compared with surgical fasciectomy particularly in the setting of a recurrence.
4	Indicated for any PIP contracture with a palpable cord.
5	Yes, this is a good case.
6	Thick cord, neurovascular bundle feels between skin and cord, patient going in wants just improvement not full correction.
7	20° to 70° contracture primary or recurrent.
8	I would consider CCH in the setting of a PIP contracture where there is a palpable cord and no independent PIP joint volar capsular contracture at the joint level that is firm/fixed. For example, if I can flex the MP joint, de-tension the cord, and we feel that the PIP contracture is mostly Dupuytren more so than PIP joint volar capsular contracture, I would consider CCH appropriate in this setting. In addition, even if the patient has a PIP volar capsular contracture, if it is a relatively "soft" PIP joint.
9	Contracture, recurrent contracture (postsurgery; post-CCH), and visible/palpable cord
10	Decent skin quality without fixed boutonnière and a palpable cord
11	Great for MP joint contractures with thick cords and as a first step for first time contractures of the MP or PIP joints
12	Preferred treatment for most PIP joints
13	The enzyme is so much simpler, easier, and safer than surgery with quicker rehab and overall costs. For patients with severe contractures or those patients with poor skin, when compared side by side, the benefits of enzymatic treatment compared with other modalities is even greater than for mild contractures. I perform collagenase injections for virtually all patients with Dupuytren with PIP contracture that need and want treatment provided that the current PIP contracture is related to Dupuytren and not a joint contracture from previous treatment with no residual DD.
14	Isolated well-defined cord, prefer MP joint contractures over PIP contractures. Diffuse disease can be problematic.
15	Just about all contractures
16	I would use CCH for most PIP flexion contractures.
17	Any MP or PIP contracture with a palpable cord
18	Palpable cord
19	Often use as initial treatment if patient has a well-developed cord and understands likely efficacy and durability outcomes

* Panelists were asked to provide open-ended responses to the question "Considering the wide-ranging nature of Dupuytren-related PIP contractures and the diversity associated with this patient population, please briefly describe the clinical scenario(s) that would lead you to use CCH in the context of Dupuytren-related PIP contractures."

severities achieved agreement consensus, indicating that these expert hand surgeons are comfortable treating most PIP joint contractures with CCH. Furthermore, these CCH experts were comfortable treating most recurrent MP and/or PIP contractures with CCH. Panelists indicated that CCH treatment was appropriate for multiple clinical scenarios in patients with Dupuytren-related PIP contracture(s), including those with two fingers, each with a PIP contracture >70° previously treated with CCH, with or without severe Dupuytren diathesis. However, agreement consensus was not reached for scenarios related to the treatment of dorsal PIP joint Garrod's nodules with unused CCH remaining after the primary injection procedure and for the attempt of PIP joint closed capsulotomy for a patient who presented initially with a 70° PIP joint contracture and was left with a 20° contracture after CCH injection and manipulation. The findings presented herein indicate that expert users agreed that CCH treatment was appropriate for most clinical scenarios proposed for patients with DD, including uses not evaluated in the CCH pivotal trials that led to US Food and Drug Administration approval.

Panelists providing feedback on the clinical scenarios presented can be considered experts in CCH administration for DD and, as such, are proficient in the administration of CCH for the treatment of DD and frequent users; however, this resulted in selection bias. Although experienced in the use of CCH, the panelists also employ conventional surgical approaches as part of the treatment armamentarium and are able to place CCH into the overall context of how to treat patients with DD. However, the focus of this survey was to obtain input regarding CCH use, not the use of needle aponeurotomy or surgical treatment of DD. Limitations include the selection of expert panelists by the steering committee and the limited number of panelists. Experienced users of CCH can provide valuable insights related to situations not commonly considered for DD treatment with CCH, including thumb contractures, more severe contractures, and use in patients receiving blood thinners. A study of 10 hand surgeons' initial cases of CCH use reported that 61.4% of 88 primary joint contractures were reduced to 0° to 5° after CCH treatment, and 85.2% of the primary joints had clinical improvement (≥50% decrease from baseline in joint contracture 30–90 days after treatment).[15] All 10 hand surgeons reported being satisfied/extremely satisfied with CCH for the treatment of DD, and all reported continued use in clinical practice.[15] Furthermore, the results of an online survey examining DD management trends among board-certified hand surgeons who were active members of the American Society for Surgery of the Hand ($n = 638$ respondents of 2,676 invitees [23.8%]) indicated that 42.9% of the respondents would treat with CCH if the patient was amenable to any treatment option.[16] In that survey, less than half of respondents preferred CCH for MP joint contractures (48.5%), MP and PIP joint contractures (35.9%), recurrent MP joint contractures (30.5%), and recurrent MP and PIP joint contractures (19.5%), although questions regarding CCH treatment for specific scenarios were not included. Differences among board-certified orthopedic surgeons, plastic surgeons, and general surgeons exist; however, these differences were not statistically significant.

Although not a focus of this report, health-economic considerations of CCH cannot be ruled out as a potential clinical decision-making factor. Some providers are opting to maximize the amount of CCH that is administered to patients with DD, consistent with the findings of the current report.[17–20] Using the entire 0.9-mg content (which differs from the US prescribing information recommendation of only using 0.58 mg of enzyme [3 CCH injections/vial])[8] offers patients the advantage of receiving a larger total dose of medication at a greater number of individual injection sites in a single visit. This approach allows the treatment of multiple joints and fingers during 1 cycle, thereby reducing the need for additional treatment visits. Approximately half of the panelists indicated that they would use CCH remaining in the vial after a procedure to treat dorsal PIP joint Garrod's nodules, although

panelists were not asked about the impetus for this decision. Future studies are warranted to examine more closely current clinical practice and factors impacting CCH use for the treatment of DD, including an economic cost-benefit analysis, comparing CCH with typical surgical treatment, if an entire vial of CCH was routinely used by providers to treat DD.

Panelist consensus that CCH is an appropriate therapeutic intervention for a wide range of patients with DD (eg, disease severity) may reassure providers managing patients with DD, particularly because a substantial subset of patients have expressed a desire for nonsurgical options for DD.[21] Overall, the findings of this comprehensive survey, using a Delphi process to achieve consensus, demonstrate that expert hand surgeons with substantial experience using CCH not only consider CCH to be an appropriate therapy for most patients with DD but also use CCH for patients with DD beyond the limits of patient types studied in the pivotal trials.

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