

Dupuytren Contracture Recurrence Following Treatment With Collagenase Clostridium Histolyticum (CORDLESS [Collagenase Option for Reduction of Dupuytren Long-Term Evaluation of Safety Study]): 5-Year Data

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Purpose Collagenase Option for Reduction of Dupuytren Long-Term Evaluation of Safety Study was a 5-year noninterventional follow-up study to determine long-term efficacy and safety of collagenase clostridium histolyticum (CCH) treatment for Dupuytren contracture.

Methods Patients from previous CCH clinical studies were eligible. Enrolled patients were evaluated annually for contracture and safety at 2, 3, 4, and 5 years after their first injection (0.58 mg) of CCH. In successfully treated joints ($\leq 5^\circ$ contracture following CCH treatment), recurrence was defined as 20° or greater worsening (relative to day 30 after the last injection) with a palpable cord or any medical/surgical intervention to correct new/worsening contracture. A post hoc analysis was also conducted using a less stringent threshold ($\geq 30^\circ$ worsening) for comparison with criteria historically used to assess surgical treatment.

Results Of 950 eligible patients, 644 enrolled (1,081 treated joints). At year 5, 47% (291 of 623) of successfully treated joints had recurrence ($\geq 20^\circ$ worsening)—39% (178 of 451) of metacarpophalangeal and 66% (113 of 172) of proximal interphalangeal joints. At year 5, 32% (198 of 623) of successfully treated joints had 30° or greater worsening (metacarpophalangeal 26% [119 of 451] and proximal interphalangeal 46% [79 of 172] joints). Of 105 secondary interventions performed in the successfully treated joints, 47% (49 of 105) received fasciectomy, 30% (32 of 105) received additional CCH, and 23% (24 of 105) received other interventions. One mild adverse event was attributed to CCH treatment (skin atrophy [decreased ring finger circumference from thinning of Dupuytren tissue]). Antibodies to clostridial type I and/or II collagenase were found in 93% of patients, but over the 5 years of follow-up, this did not correspond to any reported clinical adverse events.

Conclusions Five years after successful CCH treatment, the overall recurrence rate of 47% was comparable with published recurrence rates after surgical treatments, with one reported long-term

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treatment-related adverse event. Collagenase clostridium histolyticum injection proved to be an effective and safe treatment for Dupuytren contracture. For those receiving treatment during follow-up, both CCH and fasciectomy were elected options. (*J Hand Surg Am.* 2015; 40(8):1597–1605. Copyright © 2015 by the American Society for Surgery of the Hand. All rights reserved.)

Type of study/level of evidence Therapeutic II.

Key words Collagenase clostridium histolyticum, Dupuytren contracture, recurrence, safety.

DUPUYTREN CONTRACTURE IS A connective tissue disorder characterized by the formation of palmar nodules that can progress to form ropelike collagen cords extending into the fingers.¹ The metacarpophalangeal (MCP) joint, proximal interphalangeal (PIP) joint, or both may be affected.¹ Over time, cords can shorten and the joints become permanently contracted, resulting in deformity and impaired hand function.^{1–3} A recent population survey found that 7% of U.S. adults had symptoms or diagnosis of Dupuytren contracture, and more than a third of those affected reported their hand deformity interfered with daily activities.³

Although contracture recurrence following surgical intervention is recognized, the reported frequency of recurrence varies greatly. Reported recurrence rates range from 12% to 73% for fasciectomy/aponeurectomy and from 33% to 100% for open or needle fasciotomy/aponeurotomy.⁴ Major causes for this wide variation are the lack of clarity in descriptions and/or wide variability in definitions of recurrence, making comparisons among studies difficult.⁵ In addition, the studies reported in review articles span many decades, many different surgical techniques, and many rehabilitation protocols.

One U.S. Food and Drug Administration–approved pharmacological option for treating Dupuytren contracture is currently available. Collagenase clostridium histolyticum (CCH; Xiaflex; Auxilium Pharmaceuticals, Inc., Chesterbrook, PA) is an enzymatic treatment approved for adults with Dupuytren contracture with a palpable cord.^{6–8} CCH is also approved by the European Medicines Agency (Xiapex; Auxilium UK Limited, Windsor, UK), Swissmedic (Xiapex; Medius AG, Muttenz, Switzerland), Health Canada (Xiaflex; Actelion Pharmaceuticals Canada, Laval, Canada), and Australia Therapeutic Goods Administration (Xiaflex; Actelion Pharmaceuticals Australia, Belrose, Australia). In 2 phase 3, randomized, controlled clinical trials of patients with severe Dupuytren contracture, 44% to 64% of CCH-injected cords (0.58 mg/injection; up to 3 injections/joint) met the defined primary end point of contracture

reduction to 5° or less within 30 days of the last injection, compared with 5% to 7% of placebo-injected cords ($P < .001$).^{9,10} Adverse events (AEs) with CCH were largely localized to the injection site and resolved within 1 to 4 weeks.^{6,8}

The risk of recurrence is critical in evaluating any treatment for Dupuytren contracture. The Collagenase Option for Reduction of Dupuytren Long-Term Evaluation of Safety Study (CORDLESS) was a prospective follow-up study for patients treated with CCH in previous clinical trials. The purpose of CORDLESS was to assess long-term recurrence and safety during 5 years following treatment with CCH for Dupuytren contracture. We recently reported interim 3-year results.¹¹ At that time, of 623 joints that had previously demonstrated successful treatment (ie, $\leq 5^\circ$ contracture), 35% (217 of 623) had a recurrence ($\geq 20^\circ$ increase with a palpable cord and/or secondary surgical/medical intervention). The recurrence rate was higher in PIP joints (56%) than in MCP joints (27%). Using a clinically accepted—and more often reported—but less stringent definition of 30° or greater increase, the 3-year recurrence rate was 22% (16% MCP and 38% PIP). In the first 3 years, no new long-term or serious adverse events (SAEs) were attributable to the prior CCH treatment.¹¹ We report here final results from year 5 of CORDLESS.

MATERIALS AND METHODS

CORDLESS was a long-term, nontreatment, follow-up study conducted at 39 sites in the United States, United Kingdom, Denmark, Finland, Sweden, and Australia from 2009 through 2013. All patients were eligible to participate who had received 1 or more CCH injections and had 1 or more posttreatment assessment in previous clinical studies of CCH (9-mo open-label trials JOINT I and JOINT II¹²; 3-mo double-blind trials Collagenase Option for the Reduction of Dupuytren's (CORD) I and CORD II with 9-mo open-label extension^{9,10}). All sites had local or central institutional review board/ethics committee approval. Research was carried out in compliance with the Declaration of Helsinki as

TABLE 1. Outcomes and Definitions

Joint Classification in Phase 3 Study of Origin	Outcome Measure in CORDLESS	Criteria in CORDLESS
Successfully treated (final contracture $\leq 5^\circ$)	Recurrence of contracture	(a) $\geq 20^\circ$ increase in contracture compared with the reference value* + a palpable cord; OR (b) the joint underwent medical or surgical intervention primarily to correct new or worsening Dupuytren contracture in that joint
Measurably improved ($\geq 20^\circ$ reduction from pretreatment baseline, but final contracture $> 5^\circ$)	Nondurability of response	Same as above.
Not effectively treated (reduction of $< 20^\circ$ from pretreatment baseline)	Progression of contracture	Same as above.
Responsive (successfully treated OR measurably improved)	Worsening of contracture	(a) $\geq 20^\circ$ increase in contracture (or $\geq 30^\circ$, in <i>posthoc</i> analysis) compared with the reference value* \pm palpable cord; OR (b) the joint underwent medical or surgical intervention primarily to correct a new or worsening Dupuytren contracture in that joint.

*For successfully treated joints/recurrence, the reference value was the measurement at day 30 after the final injection in the index phase 3 study; for measurably improved joints/nondurability and for not effectively treated joints/progression, the reference value was the lesser of the measurement at day 30 or at the last evaluation in the index phase 3 study.

currently amended. Patients gave written, informed consent and could discontinue participation at any time. CORDLESS was registered on [ClinicalTrials.gov](https://clinicaltrials.gov) as NCT00954746.

Details of the study methods have been published.¹¹ Briefly, enrolled patients were followed once annually for 4 years (years 2–5 after the first injection), with 6 months or longer between visits. At each visit, investigators (ie, treating physicians) examined and measured the MCP and PIP joints of each finger and determined change in contracture. Also obtained was a history of any AEs, hand surgeries, or CCH treatments that occurred since the previous visit. Blood samples were collected for determination of antibodies to clostridial type I (AUX I) and II (AUX II) collagenase.

CORDLESS objectives and definitions

The objectives of CORDLESS were to assess, at year 2 through year 5: (1) recurrence of contracture in joints that had achieved clinical success (contracture, $\leq 5^\circ$) in the study of origin; (2) nondurability of response in joints that had shown measurable improvement (reduction from baseline, $\geq 20^\circ$) but had not achieved our definition of clinical success in the study of origin; (3) progression of contracture in joints not effectively treated (reduction from baseline, $< 20^\circ$) in the study of origin; and (4) long-term safety after CCH injections.

Criteria for recurrence, nondurability, progression, and worsening of a contracture were defined in advance

(Table 1). Recurrence (in a successfully treated joint), nondurability (in a joint that had been measurably improved), and progression (in a joint that had not been effectively treated) were defined as either (1) an increase of 20° or greater in the contracture relative to the reference value in the index phase 3 study, combined with the presence of a palpable fascial cord, or (2) a subsequent medical or surgical intervention involving the joint to correct a new or worsening contracture. (A joint with an increase of $\geq 20^\circ$ in the contracture but no palpable cord was not assessed as having recurrence/nondurability/progression, nor was a joint with a palpable cord but an increase of $< 20^\circ$). The reference value for successfully treated joints was the measurement made at day 30 after the final injection, and the reference value for other joints was the lesser of the measurements made at day 30 or the last evaluation in the study of origin. Worsening of an originally responsive contracture (ie, in a joint that was either successfully treated or measurably improved) was defined as either (1) a contracture increase of 20° or greater (regardless of whether or not a palpable cord was present), or (2) a subsequent intervention as described previously (Table 1). For the purposes of subgroup analyses, pretreatment contracture severity (ie, before CCH injection in the study of origin) was defined as either low (MCP joints, $\leq 50^\circ$; PIP joints, $\leq 40^\circ$ contracture) or high (MCP joints, $> 50^\circ$; PIP joints, $> 40^\circ$ contracture), consistent with criteria used in previous CCH studies; these designations are separate from physician ratings of baseline severity as presented in Table 2.^{9,10,12}

TABLE 2. Baseline Characteristics and Treatment Results in Study of Origin, CORDLESS vs Previous Studies

	Previous CCH Studies ^{9,10,12} (n = 950)	CORDLESS Population (n = 644)	P Value
Baseline characteristic			
Mean age, y (\pm SD)	63 (9.6)	66 (9.4)	
Male sex, n (%)	793 (84)	543 (84)	.58
White race, n (%)	949 (100)	644 (100)	—
Family history of Dupuytren, n (%)	411 (43)	279 (43)	.96
Mean age at diagnosis, y (\pm SD)	53 (12.5)	54 (12.4)	.33
Mean duration of disease, y (\pm SD)	10 (9.2)	10 (9.3)	.96
Mean number of affected joints, n (\pm SD)	2.9 (2.0)	2.8 (2.0)	.47
Type of affected joints, n (%)			.21
1 MCP/0 PIP	143 (15)	112 (17)	
\geq 2 MCP/0 PIP	141 (15)	103 (16)	
0 MCP/1 PIP	139 (15)	91 (14)	
0 MCP/ \geq 2 PIP	88 (9)	47 (7)	
\geq 1 MCP/ \geq 1 PIP	437 (46)	290 (45)	
Hands affected, n (%)			.97
One	596 (63)	404 (63)	
Both	352 (37)	239 (37)	
Physician rating of severity			.23
Mild, n (%)	202 (21)	154 (24)	
Moderate, n (%)	516 (54)	342 (53)	
Severe, n (%)	230 (24)	146 (23)	
Missing, n	2	2	
Baseline contracture of treated joints, degrees (\pm SD)	44.5 (18.7)	43.9 (18.4)	
Treatment result			
Joints treated, n	1568	1081	
MCP	920	648	
PIP	648	433	
Joints successfully treated, n (%)	838 (53)	623 (58)	
MCP (% of MCP joints treated)	618 (67)	451 (70)	
PIP (% of PIP joints treated)	220 (34)	172 (40)	
Joints measurably improved, n (%)	444 (28)	302 (28)	
MCP (% of MCP joints treated)	221 (24)	152 (23)	
PIP (% of PIP joints treated)	223 (34)	150 (35)	
Joints not effectively treated, n (%)	286 (18)	156 (14)	
MCP (% of MCP joints treated)	81 (9)	45 (7)	
PIP (% of PIP joints treated)	205 (32)	111 (26)	

In historical clinical practice, contracture of 30° or greater has been commonly used as an indication for surgery (although surgery for lesser PIP joint contractures may be considered appropriate).^{1,13} Because successfully treated joints had posttreatment contractures of 5° or less (and, therefore, an increase in contracture of \geq 30° would result in joints with \geq 30° contractures), a post hoc analysis of worsening using a threshold of 30° or

greater increase in contracture (\pm palpable cord) or medical/surgical intervention, was also performed. An increase of 30° or greater has been used previously by another group (van Rijssen et al^{14,15}) to define recurrence.

CCH dosing

In the previous clinical trials, patients could receive up to 3 injections of 0.58 mg CCH per cord (maximum of 8

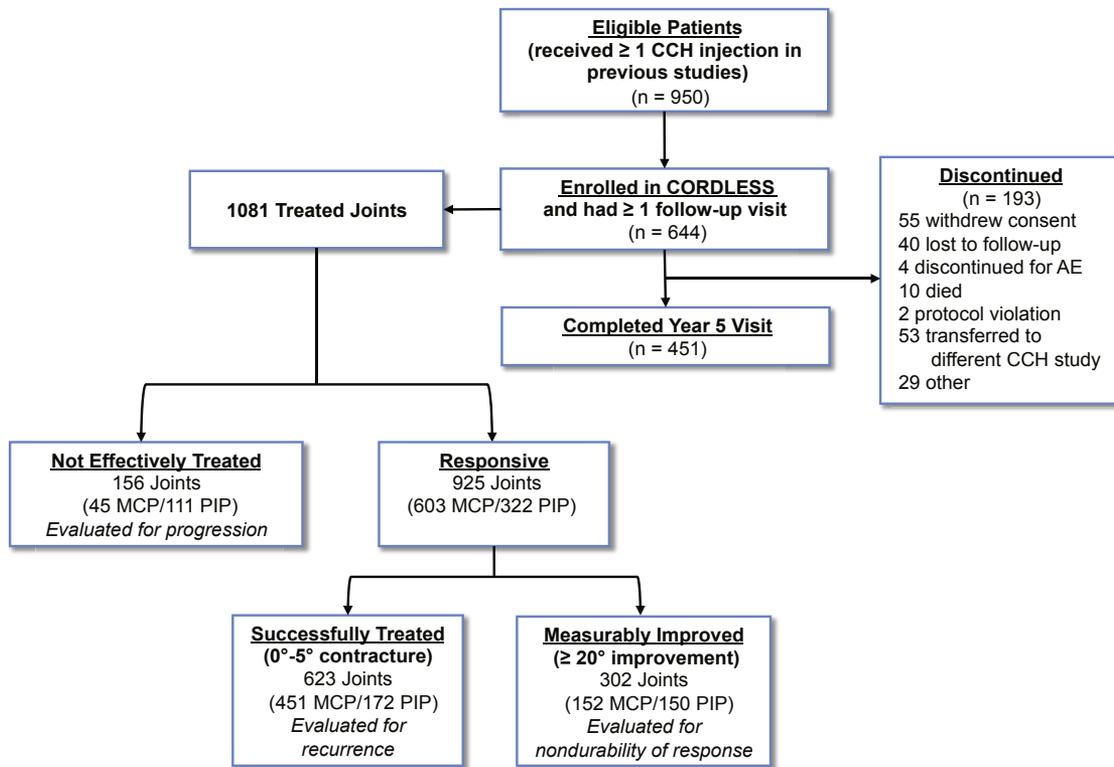


FIGURE 1: Patient disposition.

injections per patient in the study).^{9,10,12} During CORDLESS, patients could receive CCH as part of ongoing treatment by their physician (CCH became commercially available in the United States in 2010, after the year 2 visits); however, this was not mandated by the protocol. Patients treated with CCH as an intervention while enrolled in CORDLESS were monitored for AEs at each annual visit.

Statistical analyses

Demographics, disease history, and characteristics of treated joints were summarized. Characteristics of the cohort of patients/joints assessed in CORDLESS were compared with those enrolled in the prior studies to ascertain that the CORDLESS cohort was representative of the overall population (test of proportions or a 1-sample *t* test for continuous variables). Nominal incidence rates of recurrence, progression, or worsening were calculated for all joints, by joint type, and by joint type/severity; AEs, SAEs, and the causal relationship of the AE/SAE to the phase 3 CCH injection were summarized. Immunogenic responses were evaluated as anti-AUX I and anti-AUX II titers over time.

RESULTS

Of 950 eligible patients from the original studies, 644 (68%) enrolled in CORDLESS and had 1 or more

follow-up evaluations. Demographics and joint characteristics were similar for eligible and enrolled patient cohorts (Table 2). The 644 enrolled patients had 1,081 CCH-treated joints (648 MCP, 433 PIP); 623 had been successfully treated, 302 measurably improved, and 156 were not effectively treated (Fig. 1).

Successfully treated joints

The cumulative 5-year 20° or greater recurrence rate for successfully treated joints was 47% (291 of 623). The majority of recurrences (219 of 291; 75%) occurred prior to 3 years after treatment (Figs. 2 and 3).

Recurrence rates by joint type are shown in Figures 2 and 3. MCP joints of low baseline severity had a higher recurrence rate (41% [152 of 374]) compared with those of high severity (34% [26 of 77]). In contrast, low-severity PIP joints had a lower recurrence rate (63% [76 of 121]) than those of high severity (73% [37 of 51]). The mean contracture at year 5 for recurrent MCP joints (27°; *n* = 178) was less than pretreatment baseline (37°). Results were similar for recurrent PIP joints (*n* = 113) (year 5, 35°; baseline, 39°).

Using a clinically accepted threshold for surgery ($\geq 30^\circ$ contracture increase [\pm palpable cord] or medical/surgical intervention [post hoc analysis]), the rate of worsening was 32% (198 of 623) (MCP, 26% [119 of 451]; PIP, 46% [79 of 172]).

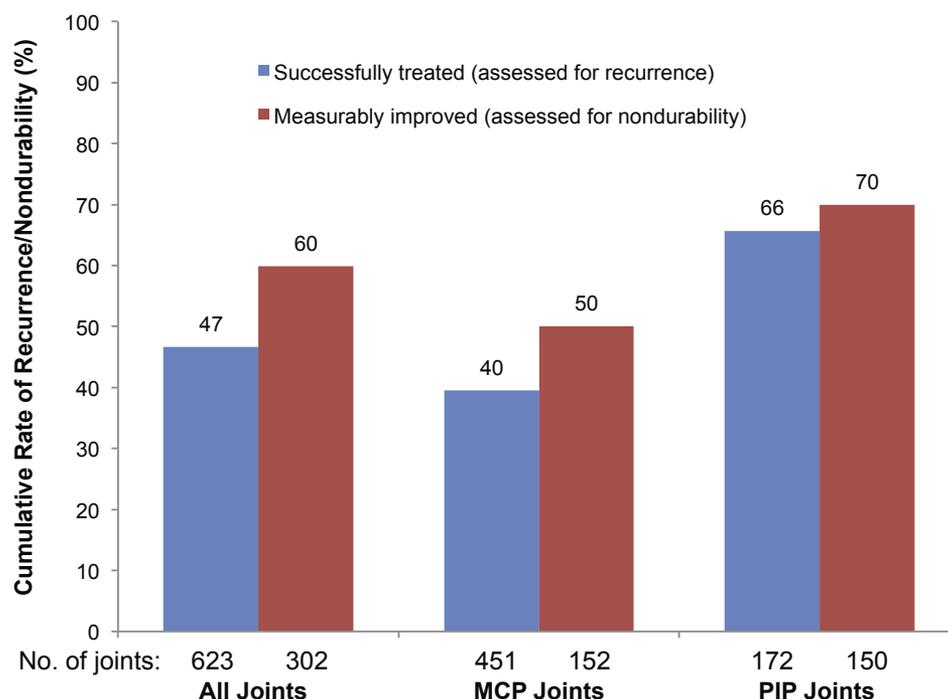


FIGURE 2: Rates of recurrence in successfully treated joints ($n = 623$ joints) and nondurability in measurably improved joints ($n = 302$ joints) at year 5 following treatment with CCH. Recurrence and nondurability were defined as contracture $\geq 20^\circ$ relative to the reference value in the presence of a palpable cord, or the joint was treated with a surgical or medical intervention to correct worsening of contracture. For successfully treated joints/recurrence, the reference value was the measurement at day 30 after the final injection in the index phase 3 study; for measurably improved joints/nondurability, the reference value was the lesser of the measurement at day 30 or at the last evaluation in the index phase 3 study.

Measurably improved joints

Rates of nondurability of response in measurably improved joints are shown in [Figure 2](#).

Responsive joints (successfully treated plus measurably improved)

Among responsive joints ($n = 925$), 48% (443 of 925) overall, 39% (234 of 603) of MCP joints, and 65% (209 of 322) of PIP joints had worsening ($\geq 20^\circ$ contracture increase [\pm palpable cord] or medical/surgical intervention). Using the threshold of 30° or greater increase, the rate of worsening was 35% (327 of 925) (MCP, 29% [174 of 603]; PIP, 48% [153 of 322]).

Joints not effectively treated

The rate of **progression** among joints that were not effectively treated was 52% (81 of 156) (MCP, 53% [24 of 45]; PIP, 51% [57 of 111]).

Medical/surgical interventions

By year 5, 16% (100 of 623) of successfully treated joints had a total of 105 medical/surgical interventions to correct worsened contractures. The most common were surgical fasciectomy (47% [49 of 105]) and CCH

injection/segmental enzymatic degradation (30% [32 of 105]) ([Fig. 4](#)). Interventions were performed in 19% (56 of 302) of measurably improved joints (combined rate of 156 of 925 [17%] among responsive joints), and in 26% (40 of 156) of joints that were not effectively treated, for a total of 18% (196 of 1081) of all treated joints.

Safety

Collagenase clostridium histolyticum treatment was not part of CORDLESS. However, during the 5-year follow-up, 66 patients received commercially available CCH treatment for any joint at the discretion of treating physicians. Among these patients, 28 experienced AEs after injection of CCH. The most common (incidence, $\geq 10\%$) were edema peripheral (12%) and contusion (11%). Most AEs were mild to moderate; 1 (skin atrophy [decrease in ring finger circumference due to thinning of Dupuytren tissue]) was considered treatment-related by investigators. During CORDLESS, 103 patients experienced SAEs (none considered treatment-related), including 10 deaths. In year 5, 93% of patients were positive for anti-AUX I antibodies and 93% for anti-AUX II antibodies; these numbers did not correspond to any clinical AEs/SAEs reported.

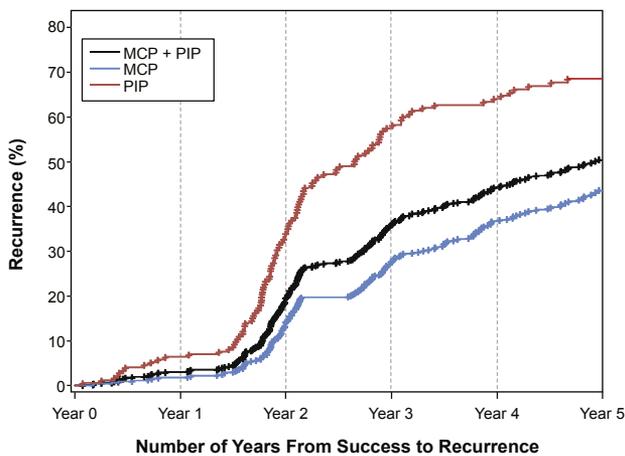


FIGURE 3: Kaplan-Meier curve for time to recurrence in joints that had been successfully treated ($n = 623$ joints). Cumulative $\geq 20^\circ$ recurrence rates were 20% for year 2, 35% for year 3, 42% for year 4, and 47% for year 5. Thus, the year-to-year increase in the rate of recurrence slowed over time (increase in years 2–3, 15%; years 3–4, 7%; years 4–5, 5%). Each plus sign indicates a reported recurrent event.

DISCUSSION

The results of this study indicate that, for 53% of joints successfully treated with CCH (to $\leq 5^\circ$ residual contracture), the response was maintained for 5 years. Even among recurrent joints, the mean contracture was less than the mean baseline contracture. As with surgical treatment, recurrence was less common in successfully treated MCP joints (40%) than in PIP joints (66%). Successfully treated PIP joints were most likely to recur if they were severely contracted prior to CCH treatment. Further investigation is required to determine if earlier treatment of PIP joints has a longer-term effect. In contrast, higher recurrence rates were observed among MCP joints of lower severity; although consistent with interim results from year 3 of follow-up,¹¹ this finding is somewhat counterintuitive. The rate of nondurability in measurably improved joints (60%) was slightly higher than the recurrence rate, indicating that joints that were more completely corrected with CCH injection initially were less likely to worsen over time.

Sixteen percent of successfully treated joints received further medical/surgical treatment over the 5-year course of follow-up. Although this percentage of retreatment appears to support a long-term response to CCH treatment, the lack of standardized indications for subsequent treatment limits our ability to draw any conclusions in this regard. CCH accounted for 30% of secondary interventions, second only to fasciectomy (47%). However, CCH was not approved by the U.S. Food and Drug Administration until after year 2 of the

study; once approved, its use increased over time and it was the second most frequently (years 3 and 5) or most frequently reported (year 4) secondary intervention.

Collagenase Option for Reduction of Dupuytren Long-Term Evaluation of Safety Study used a conservative threshold ($\geq 20^\circ$ contracture increase) for *a priori* definitions of recurrence. However, surgery has generally not been recommended until contracture is 30° or greater, especially for MCP joints,^{1,13,16} and the threshold of 30° or greater worsening to define recurrence has been used by others.^{14,15} Although our overall recurrence rate among successfully treated joints was 47%, 32% of successfully treated joints had worsening when a threshold of 30° or greater increase in contracture (or medical intervention within 5 y after initial treatment) was used.

Collagenase Option for Reduction of Dupuytren Long-Term Evaluation of Safety Study evaluated recurrence specifically in joints that had previously achieved full correction (ie, $\leq 5^\circ$ contracture). Because surgical procedures such as fasciectomy typically achieve a short-term result of full correction, this would theoretically allow relevant comparisons between recurrence rates with CCH or surgery (ie, comparing long-term outcomes based on a common starting point). However, substantial variability in published descriptions and definitions of recurrence and reported recurrence rates throughout the twentieth century largely precludes meaningful comparisons of our results with those of historical surgical studies. van Rijssen and colleagues^{14,15} also established quantitative criteria for recurrence. They used an increase of total passive extension deficit of 30° or greater compared with the 6-week follow-up values in previously treated joints. After 5 years, their recurrence rate following percutaneous needle fasciotomy (ie, a single procedure per cord) was 85% (45 of 53 treated hands); for limited fasciectomy, it was 21% (9 of 43 treated hands).¹⁵ In our study, 32% of joints successfully treated with CCH had 30° or greater worsening during 5 years of follow-up; the rate of 30° or greater worsening was slightly higher (35%) among the combined group of both successfully treated and measurably improved joints. In addition to their primary analysis, van Rijssen and colleagues^{14,15} also discussed outcomes among successfully treated joints in their study using criteria similar to those we used in CORDLESS. Successful treatment (with either limited fasciectomy or percutaneous needle fasciotomy) had been achieved in 132 (72%) MCP joints and 36 (34%) PIP joints; and among these successfully treated joints, 5-year recurrence rates following limited fasciectomy were 5% for both MCP (4 of 76) and PIP (1 of 19) joints. Following

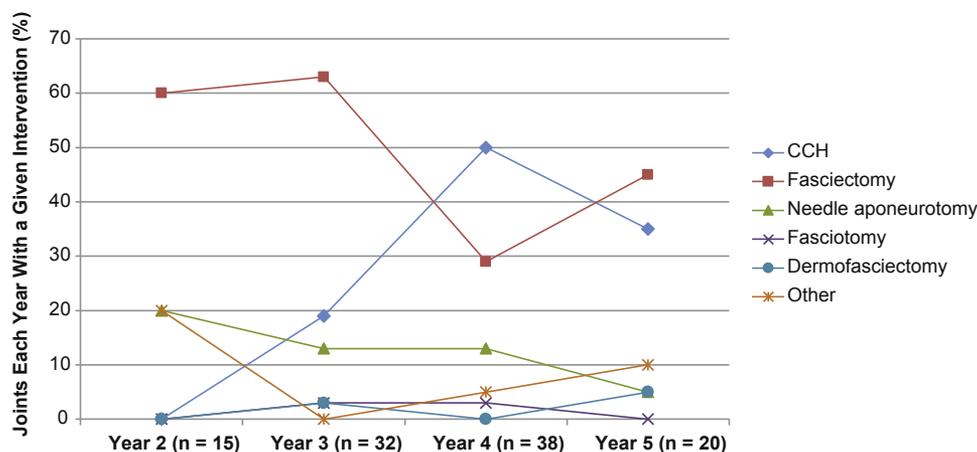


FIGURE 4: Proportion of specific types of interventions among medical/surgical interventions to correct worsening contracture in 623 joints that had been successfully treated; n, number of interventions at each year, for a total of 105. Note: CCH was not commercially available until after the year 2 visit. “Other” includes arthrodesis, cordotomy, Digit Widget, excision, PIP fusion, radiation, release, skin graft, and unknown.

percutaneous needle fasciotomy, they were 21% (12 of 55) for MCP joints and 24% (4 of 17) for PIP joints.¹⁵ However, the sample size was limited by a relatively low number of successfully treated joints, particularly for needle fasciotomy, and all patients were treated at a single site. A larger sample size from multiple study centers would be needed to fully understand the long-term efficacy of needle fasciotomy.

In CORDLESS, one third of all eligible patients failed to enroll, and 30% of those who did enroll withdrew over the course of follow-up. In some cases, patients may have been enrolled at sites that declined to participate in the follow-up study, possibly introducing site-specific bias. However, we did not detect any differences in patient or diseased joint characteristics between the eligible population and those who enrolled in CORDLESS, suggesting that the CORDLESS population was likely to be representative of the clinical study population as a whole. Finally, although it may be possible to use data from CORDLESS to identify factors associated with a long-term response to CCH treatment, these analyses were not part of the *a priori* statistical plan. Future studies may address these questions.

The safety profile of CCH appears favorable in comparison with published reports of fasciectomy, which is currently considered the standard for surgical interventions.¹⁷ A recent review that compared the incidence of AEs from CCH clinical trials (n = 1,082) and median incidence reported in published studies of fasciectomy (n = 7,727) found lower rates of nerve injury (0% vs 3.8%), neurapraxia (4.4% vs 9.4%), complex regional pain syndrome (0.1% vs 4.5%), and arterial injury (0% vs 5.5%) with CCH, whereas rates

of tendon injury were similar (0.3% vs 0.1%).¹⁸ In the first 3 years following approval of CCH in the United States approximately 49,000 injection procedures were performed; 26 tendon ruptures were reported (a rate of 0.05%), and 1 pulley injury and 1 ligament injury.¹⁹ In clinical trials and postmarketing data, most AEs associated with CCH were mild to moderate, local to the injection site, and transient.^{18,19}

In 1999, Tubiana²⁰ identified 4 characteristics of successful treatment for Dupuytren contracture: to correct deformity, avoid complications, shorten postoperative recovery, and prophylactically prevent recurrences. Short-term placebo-controlled clinical trials have demonstrated the ability of CCH to meet the first 3 criteria.^{9,10} The results of CORDLESS, in which 53% of successfully treated joints had a durable response after 5 years of follow-up, address Tubiana’s final criterion. CCH is a viable nonsurgical option for safe and effective treatment of Dupuytren contracture with recurrence rates that are now better characterized.

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5-year outcomes with post-hoc joint outcomes categorized as "success" (complete correction), "measurably improved" (correction $\geq 20^\circ$ but not complete), and "not effectively treated" (correction $\leq 20^\circ$). Post-treatment contracture progression was referred to as "recurrence", "nondurable response", and "progression" for each category respectively. Joints with contracture progression but without a palpable cord were classified as not having recurrence, nondurable response, or progression, and the number of these joints was not reported. 1081 treated joints were reported. 5 years post-treatment, 40% (258/648) of all MCP joints and 61% (266/433) of all PIP joints contracted $>20^\circ$ from their initial post-treatment measurements. The true rates are even greater considering re-contracture without a cord was not considered a recurrence. This approach marginalizes patients who don't care if their recontracture has a cord or not: a bent joint is a bent joint. The patient might ask before treatment "Doc, what are my odds of having a straight finger 5 years after treatment?". Based on the wording in this study, one might think the answer is 60% for MCP joints and 39% for PIP joints, but taking into account "measurably improved" and "not effectively treated" groups were never straight, the actual figures are 40% (273/648) for MCP joints and 14% (59/433) for PIP joints.

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