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# Durability of Collagenase Treatment for Dupuytren Disease of the Thumb and First Web After at Least 2 Years' Follow-Up

Lennart M. Steenbeek, MD,\* Marieke M. Dreise, BA,\* Paul M. N. Werker, MD, PhD\*

**Purpose** The aim of this study was to analyze the durability of the treatment results of the thumb and first web contractures in Dupuytren disease with collagenase *Clostridium histolyticum*.

**Methods** Twelve patients (14 hands) were followed for an average of 35 months (range, 24–42 months). Two patients (3 hands) were excluded, yielding 11 hands available for assessment. Nondurability was defined as a worsening of at least 20° of passive extension deficit at a treated joint or any decrease greater than 5 mm in intermetacarpal head distance, both relative to 30 days after injection or as intervention to correct new/worsening contracture. Durability was compared with that of a historic cohort of treated finger contractures.

**Results** Five out of 11 patients with a metacarpophalangeal or interphalangeal joint contracture or first web contracture had a nondurable result at an average of 35 months. Results obtained at metacarpophalangeal joints of thumbs were more durable than those of interphalangeal joints. Most of the recurrences occurred in interphalangeal joints.

**Conclusions** Treatment of thumb and first web contractures was not durable in nearly half of the cases at an average follow-up of 35 months, and durability was clearly less than that of treated finger contractures. (*J Hand Surg Am.* 2019;44(8):694.e1-e5. Copyright © 2019 by the American Society for Surgery of the Hand. All rights reserved.)

**Type of study/level of evidence** Therapeutic IV.

**Key words** Collagenase *Clostridium histolyticum*, Dupuytren disease, durability, first web, thumb.



**I**N 3% OF CASES, DUPUYTREN DEFORMITIES are located at the radial side of the hand.<sup>1</sup> In our experience, patients with thumb or first web involvement

seldom have functional problems and do not often require intervention. However, in a minority of cases, thumb function becomes severely impaired and hinders activities of daily living.<sup>2</sup>

There is a paucity of literature on the treatment of Dupuytren disease (DD) of the thumb and first web. Surgical treatment of the radial side of the hand has been reported to be more difficult than the ulnar side of the hand and needs a more extensive approach.<sup>3</sup> Tubiana<sup>3</sup> and Hueston<sup>4</sup> in such cases even advised wide dermofasciectomy and full-thickness skin grafting, especially if a high risk of recurrence is expected as in a diathesis.

Collagenase *Clostridium histolyticum* (CCH) is a mixture of 2 collagenolytic enzymes that dissolve collagen types I and III once injected in a cord. The

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During the course of the study, P.M.N.W was a member of the advisory boards of Pfizer Lts and Sobi Ltd. At present he is on the scientific advisory board of Fidia Pharma (Milan, Italy). The Department of Plastic Surgery at University Medical Centre Groningen receives his honorarium, which is used for research purposes and he is reimbursed for his travel costs. The rest of the authors declare that they have no relevant conflicts of interest.

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**TABLE 1. PED, TPED, and IMD for Thumbs and First Web**

Measurement	Mean PED MCP Joints, ° (SD)	Mean PED IP Joints, ° (SD)	Mean TPED, ° (SD)	IMD, mm (SD)
Pretreatment	28 (18)	40 (19)	43 (28)	62 (6)
30 d	3 (4)	5 (4)	11 (9)	65 (8)
3 y	16 (16)	50 (0)	33 (17)	69 (3)

treated cord is passively ruptured at least 24 hours after treatment. The efficacy and durability of CCH has been studied extensively in fingers.<sup>5–9</sup> Although CCH has been accepted in many countries as a minimally invasive treatment option,<sup>10</sup> concerns remain regarding its efficacy and cost effectiveness.<sup>11,12</sup>

The literature on the efficacy of CCH in thumbs is, however, very limited and absent on long-term durability.

We have previously reported our experience on the efficacy of CCH treatment of the thumb and first web space in 12 patients (14 hands).<sup>13</sup> We found that the 30 days posttreatment extension deficits were significantly lower than pretreatment; intermetacarpal head distances (IMDs) were significantly greater than pretreatment. These results persisted for up to 6 months follow-up in all but 1 patient.

The purpose of this study is to report longer-term durability of treatment of CCH in thumb and first web contractures. For this purpose, we followed our patients for a mean of 35 months.

## MATERIAL AND METHODS

All 12 patients with 14 hands who previously participated in the efficacy study of CCH in thumb and first web contractures<sup>13</sup> were approached an average of 35 months (range, 24–40 months) after their initial CCH treatment and asked to participate in this follow-up study. The local Medical Ethics Committee approved the study. The study was conducted according to the principles of the Declaration of Helsinki and in accordance with the Medical Research Involving Human Subjects Act (Wet Mensgebonden Onderzoek). The patients who were interested in participating expressed this by returning the informed consent form.

Our previous study<sup>13</sup> used primary DD in the thumb or first web as an inclusion criterion. To exclude dependence, the data of only 1 hand per patient were used in the analysis. Patients who had undergone additional treatment of the thumb or first web since they had received their first treatment with CCH were not excluded *a priori*. They were recorded as recurrences. At the follow-up examination, passive

extension deficit (PED) of any of the thumb joints and the IMD for first web cords were measured and total passive extension deficit of the whole thumb (TPED) calculated. A standard goniometer was used for PED,<sup>14</sup> and IMD was defined as the widest possible distance between the dorsal center of the first and second metacarpal heads in millimeters and measured using a tape measure. Because the PED of the thumb's metacarpophalangeal (MCP) and interphalangeal (IP) joints are very much influenced by the position of the carpometacarpal joint, the observer at follow-up (L.M.S.) was trained prior to this study. During this training, he examined both hands of 50 DD patients at various disease stages, without prior knowledge about location of the nodules and cords. Thereafter, his findings were cross-checked by a scientist with extensive experience in the use of the goniometer to maximize the interobserver agreement.<sup>15</sup>

Results were analyzed for recurrence, with recurrence defined as an increase of 20° of PED or greater, relative to the results achieved at 30 days posttreatment.<sup>16</sup> For IMD, no definition was available for recurrence in the literature. We arbitrarily defined it as any decrease in IMD of greater than 5 mm compared with the results achieved at 30 days after injection.

The primary outcome parameters were change of PED in degrees and IMD in millimeters.

## RESULTS

Eleven patients with DD on the radial side of their hands were available for this follow-up study (11 out of 12 patients). The included patients had a mean age of 64 years ( $\pm$  SD, 4.4) and 8 of them were men. Eight out of the 11 patients were treated in the left hand. All patients had the disease in both hands and all hands except 1 had been treated previously for DD located elsewhere in the hand, reflecting the severity of the disease in these patients. In addition, 5 patients also had Ledderhose disease.

We reanalyzed the data originating from the previous study for these 11 patients (11 hands) and summarized the analysis of efficacy in Table 1. The

CCH treatment led to an average contracture reduction of PEDs for MCP joints of 25° (SD, 15°; a reduction of 89% compared with pretreatment) at 30 days posttreatment. The IP joints achieved an average contracture reduction of 35° (88% [SD, 15°] PED. The average reduction of TPED was 32° (76% [SD, 25°]), at 30 days posttreatment. The IMDs improved from 62 mm pretreatment to 65 mm (SD, 7 mm) 30 days posttreatment.<sup>13</sup>

### Durability

In the period between 30 days and this midterm follow-up, an average of 35 months following treatment, MCP joints showed an average PED worsening of 13° (SD, 12°), and IP joints had PED worsening of 45° (SD, 0°). The IMDs improved in the same period (Table 1); it showed an average increase in distance of 4 mm (SD, 14 mm). The TPED deteriorated with an average of 22° (SD, 11°) compared with 30 days posttreatment.

Two patients, one with a contracture of the MCP joint (case 8, Table 2), the other with an IP joint contracture (case 9) showed a 20° or greater worsening in PED. In addition, 2 patients (both with an IP contracture) had experienced a debilitating worsening of their contracture and had undergone a medical/surgical correction before follow-up (cases 10 and 14). We also marked these as a recurrence.

Analysis of IMDs showed recurrence of 1 first web contracture at follow-up compared with 30 days posttreatment (case 5). The recurrence rate for all treated patients was 5 out of 11, after a mean of 35 months follow-up.

Two patients initially treated for MCP contracture (cases 7 and 12) showed also an initial improvement of IMD. This effect was lost at follow-up.

### DISCUSSION

In this follow-up study, we found that the effect of the treatment with CCH in first web contractures (IMDs) continued to be stable in most cases at a mean follow-up of 35 months after treatment. However, overall, we saw a deterioration of PED at MCP joints and IP joints, with a better durability for MCP joints than for IP joints. Notwithstanding this, 5 out of 11 patients (1 at the treated MCP joint, 3 at the treated IP joints, and 1 at the treated first web) met the definition of recurrence of contracture.

The IP joints in this study, like proximal interphalangeal (PIP) joints in other studies,<sup>17,18</sup> were found to have the least durable result. Dias et al<sup>19</sup> studied the recurrence of DD contracture of PIP joints after fasciectomy with or without full-thickness

fenestrated skin graft and found 4 patterns of evolution of finger deformity after treatment. All patients in our study had the disease in both hands, 10 out of 11 patients had been treated previously elsewhere in the hand, and most patients were treated before the age of 65 years because of severely limited thumb function. This shows that our results are in line with the progressive pattern described by Dias et al,<sup>19</sup> which suggest a more aggressive and greater volume of disease. Therefore, a higher recurrence rate than is seen in studies with CCH concerning the fingers<sup>20,21</sup> is to be expected.<sup>22</sup>

Skov<sup>12</sup> compared percutaneous needle fasciotomy with CCH for patient with a PIP joint PED of at least 20°. Most of them were treated in the little and ring finger. Inferior outcomes were seen after 2 years for CCH compared with percutaneous needle fasciotomy in terms of clinical improvement (8% vs 32%) and complications (93% vs 24%).

Abe<sup>23</sup> reported the recurrence rate after surgery performed on the radial side of the hand in 10 Japanese patients. The mean follow-up period was 4 years. Notably, recurrence did not occur. This suggests that surgery is more effective, although in their study, there were no patients with Tubiana's "malignant form" of disease.<sup>24</sup> However, they did find extension to happen mostly at the radial side of the hand.

Furthermore, the term recurrence has had various definitions in the DD literature.<sup>25</sup> Abe<sup>23</sup> used the definition of Leclercq,<sup>26</sup> which described recurrence as the reappearance of DD tissue in a zone previously operated on (and thus cleared of abnormal fascia at the time of surgery). Extension of disease was defined as appearance of new lesions in a zone previously unaffected. They did not use extension deficits as a marker of disease severity.

We used for recurrence the cutoff point of 20° in PED of a single joint as proposed in the Delphi study of Felici<sup>16</sup> in which they achieved consensus on a definition of recurrence. Badalamente and Hurst,<sup>7</sup> who developed CCH, were the first to use this cutoff point of 20°.

Because there is no definition of recurrence for first web contractures available in the literature, we arbitrarily decided to use any decrease greater than 5 mm in IMDs compared with 30 days posttreatment as the definition of recurrence for first web contractures. In addition, any patient who had undergone secondary surgical/medical intervention was scored as a recurrence.

As mentioned previously, there are limitations to comparing different interventions for DD on the radial side of the hand. Nonetheless, we feel that

**TABLE 2. PED and IMDs of All Treated Thumbs and First Web Contractures**

Hand	Type of Cord	PED MCP (°)			PED IP (°)			IMD (mm)		
		Before Injection	30 D After Injection	3 Y After Injection	Before Injection	30 D After Injection	3 Y After Injection	Before Injection	30 D After Injection	3 Y After Injection
1	First web cord	10	20	20	0	0	5	Missing	60	72
2*	First web cord	35	25	Excluded*	0	0	Excluded*	55	60	Excluded*
3	First web cord	20	0	0	0	0	0	55	55	69
4†	First web cord	20	5	Missing†	0	0	Missing†	70	70	Missing*
5	First web cord	0	0	0	0	0	0	60	75	63
6	First web cord	0	0	0	0	0	0	70	70	70
7	Pretendinous	10	0	15	10	15	20	40	75	55
8	Pretendinous	50	10	42	0	0	0	50	60	65
9	Pretendinous	40	10	0	65	10	50	55	55	64
10	Pretendinous	0	0	Reoperated	35	5	Reoperated	45	45	Reoperated
11	Pretendinous	10	0	0	0	0	0	55	55	65
12	Pretendinous	40	0	5	0	0	0	60	85	65
13†	Pretendinous	40	0	Missing†	0	0	Missing†	65	70	Missing†
14	Pretendinous	20	25	Reoperated	20	0	Reoperated	80	75	Reoperated

\*Excluded from group; treatment in both hands, 1 randomly excluded to eliminate dependence.

†Missing; lost to follow-up.

treatment with CCH for cords in thumbs and first web is an acceptable one because it is minimally invasive, has minor adverse events, has a short recovery time, and gives acceptable results. The clear disadvantages are its high cost and the high recurrence rate.

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