

# Collagenase Clostridium Histolyticum versus Limited Fasciectomy for Dupuytren's Contracture: Outcomes from a Multicenter Propensity Score Matched Study

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**Background:** Controversy exists about the relative effectiveness of injectable collagenase (collagenase clostridium histolyticum) and limited fasciectomy in the treatment of Dupuytren's contracture. The authors compared the effectiveness of both techniques in actual clinical practice.

**Methods:** This study evaluated all subjects treated with collagenase clostridium histolyticum or limited fasciectomy for metacarpophalangeal and/or proximal interphalangeal joint contractures between 2011 and 2014 at seven practice sites. The authors compared the degree of residual contracture (active extension deficit), Michigan Hand Outcomes Questionnaire scores, and adverse events at follow-up visits occurring between 6 and 12 weeks after surgery or the last injection with the use of propensity score matching.

**Results:** In 132 matched subjects who were treated with collagenase ( $n = 66$ ) or fasciectomy ( $n = 66$ ), the degree of residual contracture at follow-up for affected metacarpophalangeal joints was not significantly different (13 degrees versus 6 degrees;  $p = 0.095$ ) and affected proximal interphalangeal joints had significantly worse residual contracture in the collagenase group compared with those in the fasciectomy group (25 degrees versus 15 degrees;  $p = 0.010$ ). Collagenase subjects experienced fewer serious adverse events than did fasciectomy subjects and reported larger improvements in the Michigan Hand Outcomes Questionnaire subscores evaluating satisfaction with hand function, activities of daily living, and work performance.

**Conclusions:** This propensity score–matched study showed that collagenase clostridium histolyticum was not significantly different from limited fasciectomy in reducing metacarpophalangeal joint contractures, whereas proximal interphalangeal joint contractures showed slightly better reduction following limited fasciectomy. Collagenase provided a more rapid recovery of hand function than did fasciectomy and was associated with fewer serious adverse events. (*Plast. Reconstr. Surg.* 136: 87, 2015.)

**CLINICAL QUESTION/LEVEL OF EVIDENCE:** Therapeutic, III.

**D**upuytren's disease is an incurable fibroproliferative disease involving the palmar fascia of the hand. Abnormal deposition of collagen initially leads to the formation of palpable palmar nodules. As the disease progresses, cords typically develop that cause flexion contractures

at the affected finger joints. Ultimately, these contractures can severely impair hand function and diminish quality of life.<sup>1</sup>

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*Presented in part at the 2015 Annual Meeting of the American Association for Hand Surgery, in Paradise Island, Bahamas, January 21 through 24, 2015.*

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DOI: 10.1097/PRS.0000000000001320

**Disclosure:** *The authors declare that several coauthors (S.E.R.H., R.W.S., and R.F.) have been consultants to Pfizer and Sobi, two manufacturers of injectable collagenase in Europe, after agreeing not to personally receive any form of financial compensation for their advisory services. Support was received from Pfizer in the form that the injections used in the present study were provided free of charge. However, the present study was conducted without any involvement from either pharmaceutical company to ensure objectivity.*

Collagenase clostridium histolyticum, which selectively disintegrates collagen, is a recently popularized enzymatic treatment option for Dupuytren's contracture.<sup>2</sup> The technique involves the injection of a small volume of collagenase solution into the pathologic cord(s), thus weakening the treated areas to allow for subsequent rupture by manipulation of the contracted finger. Although several large clinical trials have demonstrated the efficacy<sup>2</sup> ( $n = 308$ ) and safety<sup>3</sup> ( $n = 587$ ) of the injections, these studies were placebo-controlled,<sup>4</sup> and therefore do not provide evidence on the relative effectiveness of collagenase clostridium histolyticum and the available surgical techniques.

Limited fasciectomy remains the most widely accepted surgical standard of care for Dupuytren's disease. As of this writing, few studies have directly compared limited fasciectomy with collagenase clostridium histolyticum: the only two comparative studies we are aware of reported that the two techniques were similar in reducing joint contractures.<sup>5,6</sup> However, these studies had relatively small sample sizes ( $n = 46$  in the largest study), which may have precluded the authors from finding significant differences because of limited statistical power. Another weakness inherent in such observational studies relates to the risk of confounding by indication. Because the choice of performing collagenase clostridium histolyticum and limited fasciectomy is influenced partly by patient and clinical characteristics, such as diathesis factors, severity of the disease, and the joint levels involved, these should be accounted for to ensure valid comparisons between treatment groups.

The purpose of this study was to directly compare the early clinical results of collagenase clostridium histolyticum and limited fasciectomy while minimizing the risk of confounding by indication bias with the use of propensity score matching. Propensity score matching is a statistical approach that allows investigators to account for a large number of observed confounding variables, and is particularly useful in circumstances where randomized treatment allocation is unfeasible or unethical.<sup>7</sup> Because randomized clinical trials evaluating collagenase clostridium histolyticum versus limited fasciectomy are currently lacking, this approach allowed for a timely comparison of the effectiveness of both techniques in reducing contractures and restoring hand function in actual clinical practice.<sup>8</sup>

## PATIENTS AND METHODS

After approval of the study by the Erasmus MC Medical Ethics Committee, all subjects with

Dupuytren's disease undergoing collagenase clostridium histolyticum and limited fasciectomy between August of 2011 and March of 2014 at seven practice sites in The Netherlands were identified using a prospectively maintained database. Patient characteristics derived from this database were age, sex, hand dominance, and comorbidities. Disease-specific characteristics included bilateral presence of the disease, primary versus recurrent disease, and family history of Dupuytren's disease. In case data were missing from the database, electronic health records were abstracted.

Subjects with the diagnosis of Dupuytren's disease, aged 18 years or older, and with the ability to complete the study questionnaires in Dutch were included in the study. Exclusion criteria included multiple finger involvement, concomitant hand conditions or interventions (e.g., carpal tunnel release) on the affected side, and the lack of baseline data on the degree of contracture. Subjects undergoing revision treatment for recurrent disease were included if other eligibility criteria were met. This study was conducted in accordance with the Declaration of Helsinki.

## Treatments

Treatments were performed as part of routine care by the hand surgeons of the seven sites through shared decision-making. Collagenase clostridium histolyticum was administered according to the manufacturer's instructions, without local anesthesia. Injections were limited to 0.25 ml and 0.20 ml for metacarpophalangeal and proximal interphalangeal joint contractures, respectively. Compressive dressings were applied afterward. Treated fingers were manipulated after 24 to 72 hours to attempt rupturing of the weakened cords under local anesthesia. Up to three injections were offered at 4-week intervals if subjects were dissatisfied with the achieved level of contracture correction, but were not mandatory.

Limited fasciectomy, which is the preferred technique for treating Dupuytren's disease in The Netherlands,<sup>9</sup> was performed with tourniquet exsanguination and loupe magnification under axillary block or general anesthesia in an operating theater. Cords were approached and excised after Bruner type or longitudinal incisions with Z-plasties. Care was taken to prevent injury to the digital neurovascular bundles. Compressive dressings were applied for 2 weeks. All patients were offered a similar supervised program of hand therapy with instructed use of removable night splints for 3 months.

### Outcome Assessments

The primary outcome of this study was the degree of residual contracture assessed at follow-up visits occurring between 6 and 12 weeks after surgery or the last injection. Certified hand therapists performed goniometry to determine the degree of active extension deficit at baseline and follow-up according to a standardized assessment protocol. Hyperextension was classified as 0 degrees to prevent underestimation of extension deficit.

Secondary outcomes assessed included whether affected joints achieved clinical improvement (defined as >50 percent reduction from baseline contracture), adverse events, and self-reported hand function assessed using the Michigan Hand Outcomes Questionnaire. The questionnaire is a self-reported functioning scale consisting of 37 items evaluating six functional subdomains for each hand separately: overall hand function, ability to perform activities of daily living, work performance, aesthetics, pain, and satisfaction with hand function. It has been rigorously designed and used for a variety of hand conditions,<sup>10</sup> including Dupuytren's disease.<sup>11,12</sup> Scores range from 0 (poorest function) to 100 (best function). Because functional restoration was considered the primary treatment objective, we excluded all pain outcomes from our analysis. Only the outcomes pertaining to the treated side were used. Adverse events were graded based on their severity into two categories: serious (non-transient or requiring an intervention) and mild (transient or not requiring an intervention).

Given the increasing clinical and policy implications of patient satisfaction data,<sup>13</sup> we performed a post hoc analysis of the specific items that constitute the satisfaction subdomain of the Michigan Hand Outcomes Questionnaire. These items examine satisfaction with overall hand function, finger motion, wrist motion, hand strength, and sensation, and are assessed using a five-point Likert scale, with possible answers ranging from "very satisfied" (one point) to "very dissatisfied" (five points). Subjects who rated their satisfaction as "very satisfied" (one point) or "somewhat satisfied" (two points) were classified as "satisfied" and all others were classified as "dissatisfied."

### Statistical Analysis

Continuous variables were reported as means  $\pm$  SD and categorical variables were summarized with the use of frequencies. Sample-size calculations revealed that a total of 32 metacarpophalangeal contractures (16 each group) and 70

proximal interphalangeal contractures (35 each group) would provide 80 percent power ( $\beta = 0.20$ ,  $\alpha = 0.05$ ) to detect a 10-degree difference in residual contracture between the two treatment groups with the use of two-sided tests.

Propensity score matching was used to minimize the risk of confounding by indication bias.<sup>14</sup> The propensity score was defined as the probability of receiving collagenase clostridium histolyticum conditional on eight baseline factors. We used logistic regression modeling to estimate a score for each subject with the treatment type as the independent variable and the following baseline variables as dependent variables: age, sex, family history of Dupuytren's disease, bilateral involvement, recurrent disease, and degree of contracture at the three joint levels. The scores were then used to match collagenase subjects to limited fasciectomy subjects on a one-to-one basis using a nearest-neighbor algorithm while allowing for a matching tolerance width of 0.2 SD of the logit of the propensity score. We excluded unmatched subjects from further analysis. To examine whether the matching approach improved balance among the matched treatment groups, significance testing was performed.

For joint contracture and Michigan Hand Outcomes Questionnaire outcomes, we used a mixed-models repeated measures approach to compare the change from baseline with least-square means and corresponding standard errors plotted graphically. An advantage is that this approach estimates missing values and accounts for the within-subject dependency of the repeated measures.<sup>15,16</sup> Joint contracture was evaluated separately for affected metacarpophalangeal and proximal interphalangeal joints.

Our primary outcome analysis included all affected joints. However, in some collagenase subjects with two affected joints in the same finger, one of the contractures was specifically treated with collagenase clostridium histolyticum (mostly metacarpophalangeal) because the degree of contracture of the other affected joint was improved to such an extent that further injections were deemed unnecessary.<sup>2</sup> To assess whether the inclusion of all affected joints in our analysis influenced our results, we performed a subgroup analysis of only the primary targeted joint contractures.

The incidence of serious adverse events was compared between the groups using the Fisher's exact test. Mild adverse events were not compared because many of these were considered to be collagenase clostridium histolyticum specific or a natural consequence of surgery. Significance

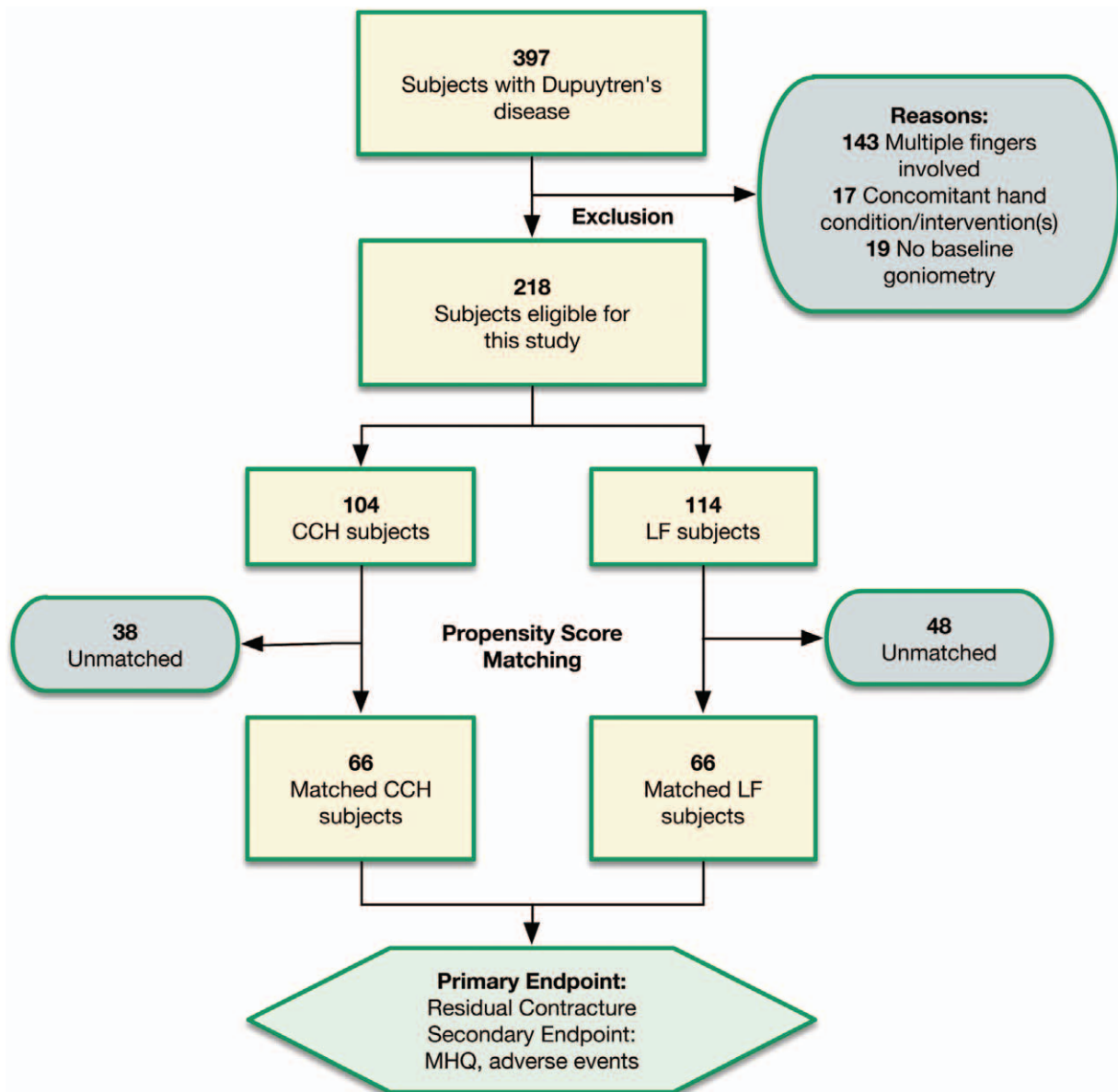
thresholds were set at  $p < 0.05$ . Statistical analyses were performed using R (version 2.14) and IBM SPSS, Version 20.0 (IBM Corp., Armonk, N.Y.).

### RESULTS

There were a total of 397 subjects with Dupuytren's disease who were treated with collagenase clostridium histolyticum or limited fasciectomy by one of the 15 surgeons of the practice sites. To improve comparability between the two treatment groups, 36 percent of the subjects who underwent limited fasciectomy for contractures involving multiple fingers were excluded. After exclusion

of another 9 percent of subjects because of the other criteria, there remained a total of 218 eligible subjects, of whom 48 percent were treated with collagenase and 52 percent were treated with fasciectomy (Fig. 1).

Table 1 shows the baseline characteristics of the study sample before and after propensity score matching. Before matching, the collagenase clostridium histolyticum group had relatively milder proximal interphalangeal and distal interphalangeal joint contractures but worse metacarpophalangeal joint contractures. In addition, the proportion of subjects treated for recurrent disease was smaller in the collagenase



**Fig. 1.** Subject selection flowchart. CCH, collagenase clostridium histolyticum; LF, limited fasciectomy; MHQ, Michigan Hand Outcomes Questionnaire.

group and the distribution of the involved fingers was different. Using propensity scores, we were able to match 66 collagenase subjects with mean baseline contractures of 39 degrees for 43 affected metacarpophalangeal joints and 41 degrees for 43 affected proximal interphalangeal joints to 66 fasciectomy subjects with mean baseline contractures of 39 degrees for 39 affected metacarpophalangeal joints and 41 degrees for 52 affected proximal interphalangeal joints with similar characteristics.

Ninety-six percent of affected joints in the matched limited fasciectomy group had follow-up data available, compared with 80 percent in the matched collagenase clostridium histolyticum group. Follow-up duration for the treatment groups was on average 11 weeks (range, 6 to 12 weeks) and was not significantly different between groups.

### Joint Contracture

For affected metacarpophalangeal joints, the degree of residual contracture (collagenase clostridium histolyticum, 13 degrees; limited fasciectomy, 6 degrees) (Fig. 2, *left*) at follow-up and the proportion of joints achieving clinical improvement (Fig. 3, *above*) were not significantly different between the matched treatment groups.

For affected proximal interphalangeal joints, however, the degree of residual contracture was significantly worse in the collagenase group than in the fasciectomy group (collagenase clostridium histolyticum, 25 degrees; limited fasciectomy, 15 degrees) (Fig. 2, *right*). In line with this, relatively fewer affected proximal interphalangeal joints achieved clinical improvement in the collagenase group than in the fasciectomy group (Fig. 3, *below*).

### Self-Reported Outcome

Michigan Hand Outcomes Questionnaire (sub)scores at baseline were similar among the matched treatment groups. Collagenase clostridium histolyticum subjects reported significantly larger improvements than did limited fasciectomy subjects in the subdomain scores assessing satisfaction, activities of daily living, and work performance (Fig. 4).

The proportion of subjects who were satisfied with each of the items that make up the satisfaction subdomain of the questionnaire was similar between the matched treatment groups at baseline (Fig. 5). The proportion of subjects who were satisfied with their finger mobility and hand

function had similarly increased at follow-up in the two treatment groups. However, as compared with fasciectomy subjects, more collagenase subjects were satisfied with their hand strength and sensation.

### Adverse Events

Table 2 lists the adverse events noted in the matched groups, graded by severity. All serious adverse events occurred after limited fasciectomy; three events of tenosynovitis requiring an intervention and one nerve injury were noted as compared with zero events after collagenase clostridium histolyticum ( $p = 0.042$ ). Arterial injuries, cold intolerance complaints, and tendon ruptures were not seen in either of the matched groups. Three of the most frequently noted mild adverse events after collagenase were peripheral edema (74 percent), contusion (64 percent), and extremity pain (26 percent).

### Subgroup Analysis of the Joints Affected by Recurrent Disease

Evaluating only the joints affected by recurrent disease, we found no significant differences in the baseline degree of contracture among the matched treatment groups, although affected metacarpophalangeal joints were on average 8 degrees worse in the collagenase clostridium histolyticum subgroup than in the limited fasciectomy subgroup.

Comparison of these two groups showed that although the degree of residual contracture at follow-up was not significantly different for affected metacarpophalangeal joints (collagenase clostridium histolyticum, 19 degrees; limited fasciectomy, 10 degrees) (Fig. 6, *left*), affected proximal interphalangeal joints in the collagenase subgroup were significantly worse compared with those in the fasciectomy subgroup (collagenase clostridium histolyticum, 33 degrees; limited fasciectomy, 22 degrees) (Fig. 6, *right*).

### Subgroup Analysis of Primary Targeted Joints

Evaluation of only the joints that were specifically targeted with collagenase clostridium histolyticum also showed a similar degree of residual contracture compared with all affected metacarpophalangeal joints in the limited fasciectomy group (data not shown). However, the proximal interphalangeal joint contractures that were specifically targeted with collagenase clostridium histolyticum showed significantly worse residual contracture compared with the fasciectomy group.

**Table 1. Baseline Characteristics before and after Propensity Score Matching, by Treatment Group\***

|  | All Subjects |         |          | Matched Subjects |         |          |
|--|--------------|---------|----------|------------------|---------|----------|
|  | CCH          | LF      | <i>p</i> | CCH              | LF      | <i>p</i> |
| No. of patients                                | 104          | 114     |          | 66               | 66      |          |
| Demographics                                   |              |         |          |                  |         |          |
| Age, yr  | 61 ± 10      | 63 ± 9  | 0.410    | 61 ± 10          | 63 ± 8  | 0.334    |
| Male sex, %                                    | 80           | 81      | 0.868    | 82               | 76      | 0.394    |
| Diabetes, %                                    | 3            | 9       | 0.087    | 6                | 5       | 0.698    |
| Current tobacco use, %                         | 9            | 16      | 0.090    | 8                | 15      | 0.170    |
| Disease characteristics, %                     |              |         |          |                  |         |          |
| Recurrent disease                              | 26           | 38      | 0.063    | 33               | 30      | 0.709    |
| Bilateral disease                              | 85           | 83      | 0.797    | 89               | 89      | 1.000    |
| Treated side is dominant                       | 58           | 53      | 0.453    | 53               | 61      | 0.380    |
| Positive family history of Dupuytren's disease | 54           | 60      | 0.388    | 59               | 49      | 0.222    |
| Treated finger, %                              |              |         | 0.003    |                  |         | 0.789    |
| Little   | 48           | 72      |          | 55               | 61      |          |
| Ring   | 37           | 24      |          | 33               | 32      |          |
| Other  | 15           | 4       |          | 12               | 8       |          |
| Outcomes                                       |              |         |          |                  |         |          |
| Contracture, degrees†                          |              |         |          |                  |         |          |
| MP joint                                       | 29 ± 24      | 19 ± 27 | 0.002    | 26 ± 25          | 23 ± 25 | 0.632    |
| PIP joint                                      | 22 ± 25      | 44 ± 27 | <0.001   | 27 ± 26          | 33 ± 25 | 0.221    |
| DIP joint                                      | 1 ± 4        | 8 ± 14  | <0.001   | 1 ± 14           | 2 ± 14  | 0.547    |
| Total MHQ score (0–100)                        | 75 ± 14      | 74 ± 15 | 0.844    | 77 ± 13          | 75 ± 14 | 0.545    |

CCH, collagenase clostridium histolyticum; LF, limited fasciectomy; MP, metacarpophalangeal; PIP, proximal interphalangeal; DIP, distal interphalangeal; MHQ, Michigan Hand Outcomes Questionnaire.

\*Plus-minus values are means ± SD.

†Values are reported for all joints.

## DISCUSSION

The aim of this study was to compare the effectiveness of collagenase clostridium histolyticum and limited fasciectomy and to account for the baseline variables that contribute to treatment

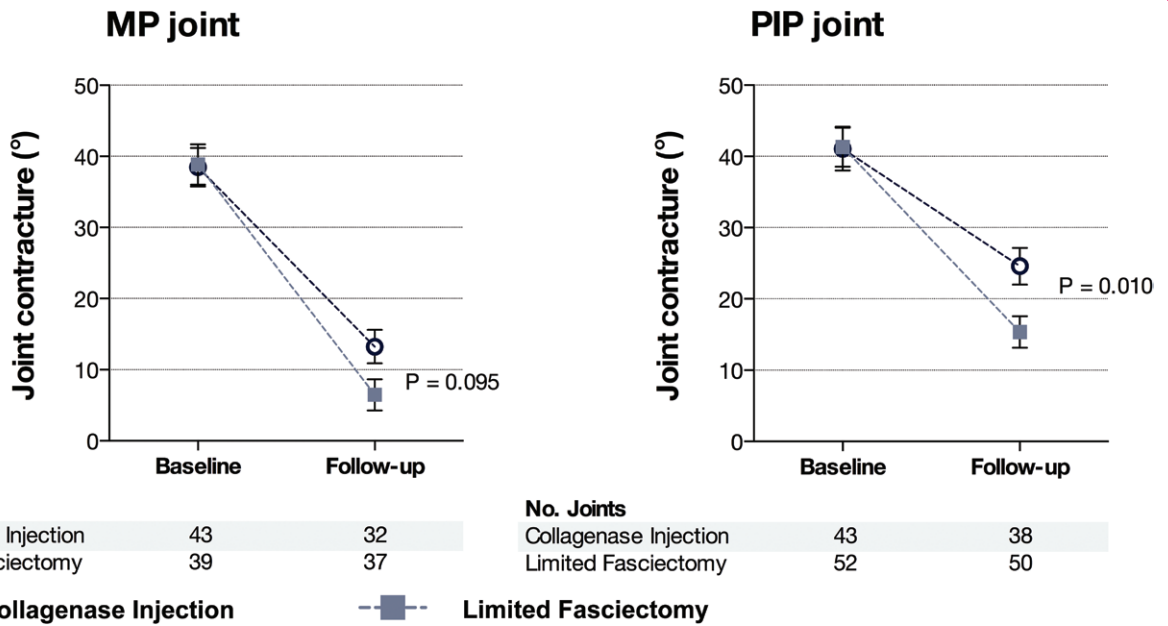
selection bias using propensity score matching.<sup>17</sup> Our primary finding was that the degree of residual contracture in the two treatment groups was not significantly different for contractures at the metacarpophalangeal joint level, whereas affected proximal interphalangeal joints showed a relatively small but significantly worse residual contracture in the collagenase group compared with the fasciectomy group. Nevertheless, subjects in the collagenase group reported larger functional improvements than did fasciectomy subjects at early follow-up, and experienced fewer serious adverse events.

Previous comparative studies on collagenase clostridium histolyticum have reported 10 degrees of residual contracture for affected metacarpophalangeal joints<sup>6,18</sup> and 23 and 26 degrees of residual contracture for affected proximal interphalangeal joints<sup>6,18</sup> at early follow-up, which is similar to the 13 and 24 degrees found in the present study. The 6 and 15 degrees for affected metacarpophalangeal and proximal interphalangeal joints found in our fasciectomy group is consistent with the 5 and 14 degrees reported at 6-week follow-up by van Rijssen and colleagues.<sup>19</sup> However, our finding that limited fasciectomy was superior to collagenase clostridium histolyticum for affected proximal interphalangeal joints contrasts the few available studies comparing the two techniques.<sup>5,6</sup> Although one retrospective study

**Table 2. Adverse Events, by Matched Treatment Groups**

|                     | CCH (%) | LF (%) |
|---------------------|---------|--------|
| No. of patients     | 66      | 66     |
| Adverse event       |         |        |
| Serious             |         |        |
| Tenosynovitis       | 0 (0)   | 3 (5)  |
| Nerve injury        | 0 (0)   | 1 (2)  |
| Arterial injury     | 0 (0)   | 0 (0)  |
| Tendon rupture      | 0 (0)   | 0 (0)  |
| Cold intolerance    | 0 (0)   | 0 (0)  |
| CRPS                | 0 (0)   | 0 (0)  |
| Mild                |         |        |
| Peripheral edema    | 49 (74) | n.a.   |
| Contusion           | 42 (64) | n.a.   |
| Extensive           | 3 (5)   | n.a.   |
| Mild                | 39 (59) | n.a.   |
| Pain in extremity   | 17 (26) | n.a.   |
| Blood blister       | 9 (14)  | n.a.   |
| Skin fissure        | 5 (8)   | 0 (0)  |
| Paresthesia         | 3 (5)   | 3 (5)  |
| Axillary tenderness | 6 (9)   | n.a.   |
| Erythema            | 3 (5)   | n.a.   |
| Wound dehiscence    | 0 (0)   | 2 (3)  |
| Pruritus            | 3 (5)   | n.a.   |
| Lymphadenopathy     | 2 (3)   | n.a.   |
| Neurapraxia         | 0 (0)   | 1 (2)  |
| Flare reaction      | 1 (2)   | 0 (0)  |

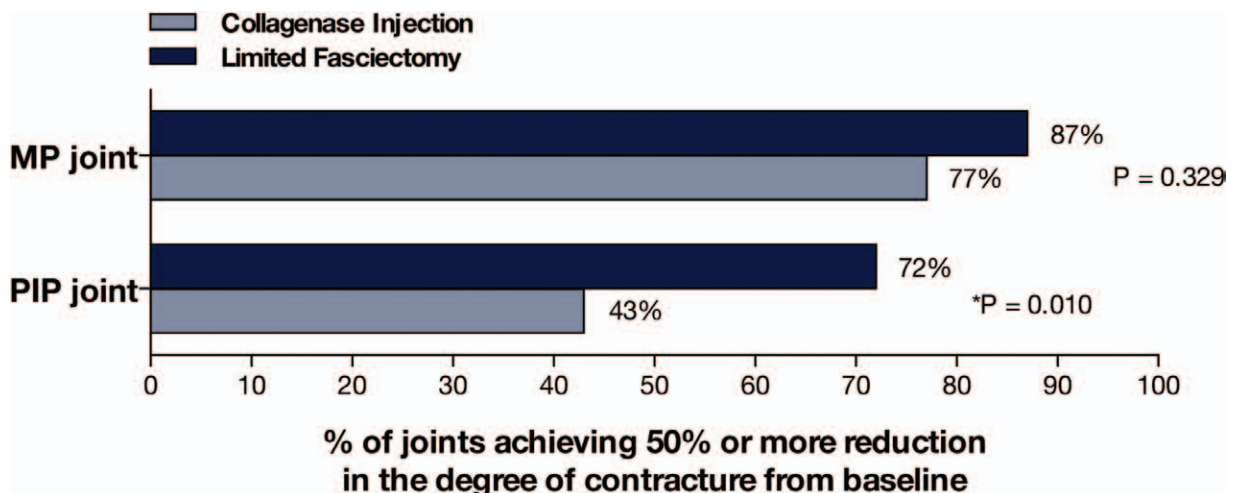
CCH, collagenase clostridium histolyticum; LF, limited fasciectomy; CRPS, complex regional pain syndrome; n.a., not assessed.



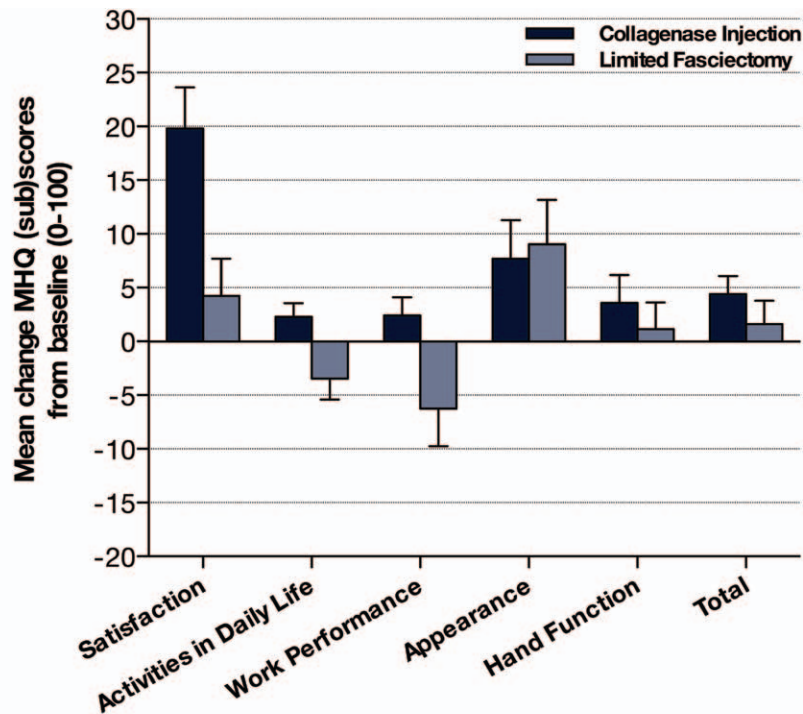
**Fig. 2.** Degree of contracture for affected metacarpophalangeal (*left*) and proximal interphalangeal (*right*) joints in the matched collagenase injection and limited fasciectomy groups at baseline and follow-up. Least-square means and standard errors from a repeated measures model are plotted. *MP*, metacarpophalangeal; *PIP*, proximal interphalangeal.

found that limited fasciectomy achieved an average of 9 degrees more contracture reduction after examining a total number of 24 affected proximal interphalangeal joints, this difference was not significant.<sup>18</sup> The only other head-to-head study of which we are aware reported similar results after evaluating only 18 affected proximal interphalangeal joints.<sup>6</sup> In contrast, the present study included more subjects with proximal interphalangeal joint involvement and was therefore more powered to detect significant differences. Another reason may be that the two procedures differ fundamentally:

collagenase clostridium histolyticum is a closed technique that relies on enzymatic fasciotomy, whereas an open technique such as limited fasciectomy allows for extensive excision of the cord and the performance of ancillary surgical efforts, such as the division of the collateral ligaments and checkrein ligaments and occasionally the release of the volar plate, to maximize joint correction. However, it should also be noted that the results in the collagenase group reflect the injection technique as recommended by the manufacturer, that is, injecting in only one part of the cord. Injection



**Fig. 3.** Percentage of affected joints meeting clinical improvement, defined as more than 50 percent improvement from baseline in the degree of contracture. *MP*, metacarpophalangeal; *PIP*, proximal interphalangeal.



**Change in MHQ score**

|                       |        |        |        |       |       |       |
|-----------------------|--------|--------|--------|-------|-------|-------|
| Collagenase Injection | 19.8   | 2.3    | 2.4    | 7.7   | 3.6   | 4.4   |
| Limited Fasciectomy   | 4.2    | -3.5   | -6.3   | 9.0   | 1.2   | 1.6   |
| P Value               | *0.003 | *0.033 | *0.029 | 0.821 | 0.506 | 0.363 |

**Fig. 4.** Change in Michigan Hand Outcomes Questionnaire (MHQ) scores in the matched collagenase injection and limited fasciectomy groups at follow-up as compared with baseline. Asterisks denote significant differences between the matched treatment groups.

into multiple areas, as recently suggested by Murphy and colleagues, may translate into better results at the proximal interphalangeal joint level and should be explored in future investigations.<sup>8</sup>

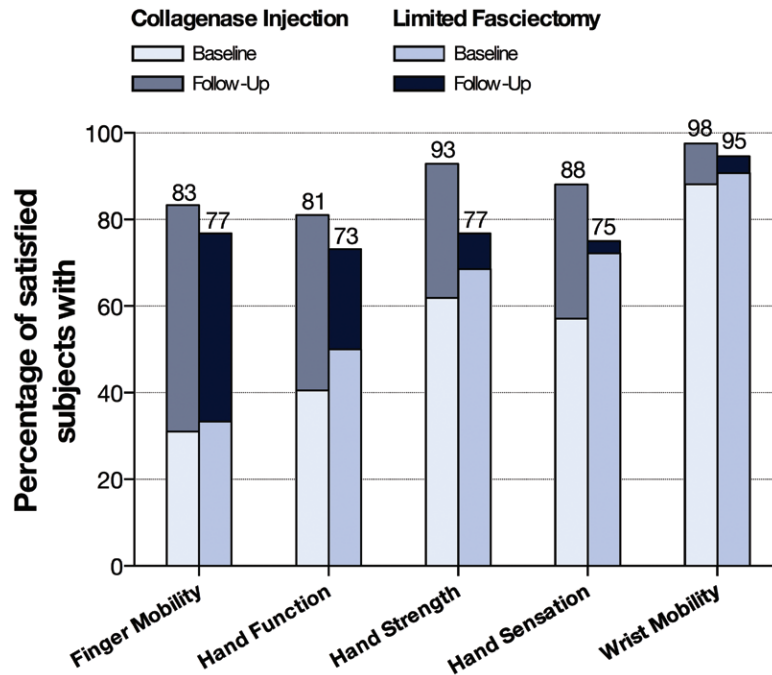
As compared with those who underwent limited fasciectomy, collagenase clostridium histolyticum subjects reported larger functional improvements in the Michigan Hand Outcomes Questionnaire subdomains assessing activities of daily living, work performance, and satisfaction with hand function at follow-up. As a recent study reported a gradual improvement in questionnaire scores in the first year following limited fasciectomy,<sup>12</sup> we believe that this finding primarily shows that hand function recovers more rapidly after collagenase clostridium histolyticum than after limited fasciectomy, which is consistent with what was previously reported by an observational study that used the Disabilities of the Arm, Shoulder, and Hand questionnaire.<sup>5</sup>

This study has several limitations. Although most previous reports evaluated only primary cases, our study included subjects with joints affected by

primary and recurrent disease. Although our subgroup analysis of only the subjects with recurrent disease showed that the comparative effectiveness of the two techniques was similar to that of the overall groups, future studies with a larger number of recurrent cases are required to confirm these findings. Moreover, the relatively higher incidence of serious adverse events noted in the limited fasciectomy group warrants careful interpretation because of the small number of events but is in line with a previous systematic review showing that collagenase clostridium histolyticum has a more favorable risk profile than limited fasciectomy.<sup>20</sup>

Another concern is that our study evaluated only early clinical results, leaving uncertainty about the durability of these outcomes. However, we decided on this approach because, as of this writing, few studies have directly compared collagenase clostridium histolyticum to limited fasciectomy in terms of their associated risks and their effectiveness in reducing contractures and restoring hand function. Although studies have shown acceptable long-term outcomes for each

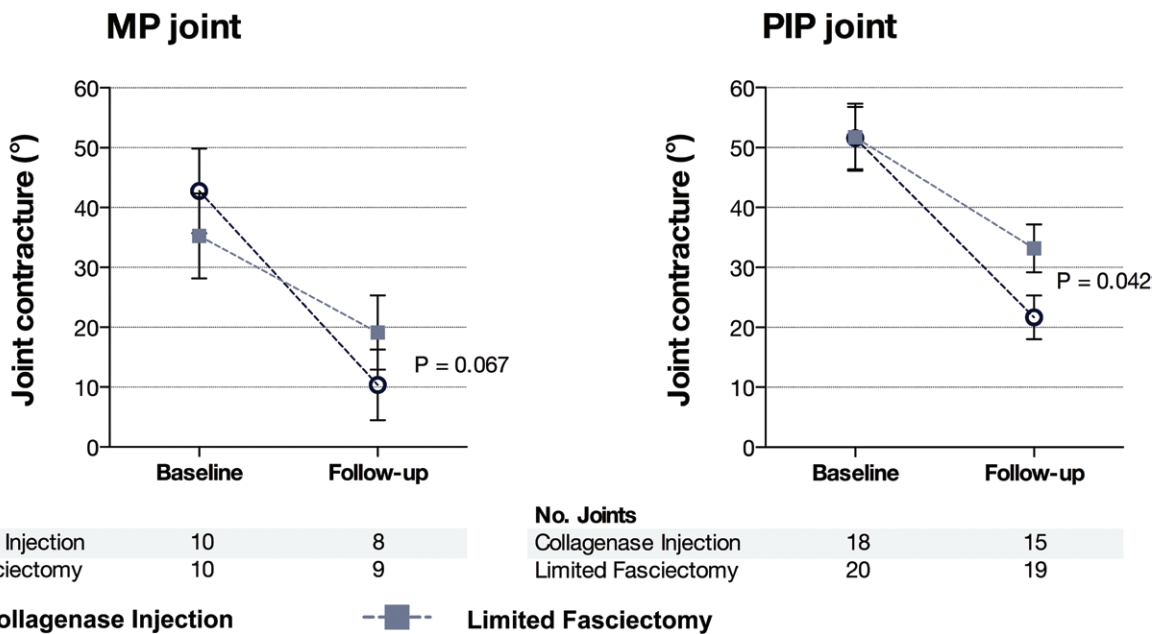




**% Increase from baseline**

|                       |    |    |    |    |   |
|-----------------------|----|----|----|----|---|
| Collagenase Injection | 52 | 41 | 31 | 31 | 9 |
| Limited Fasciectomy   | 44 | 23 | 8  | 3  | 4 |

**Fig. 5.** The proportion of subjects who were satisfied with five specific items constituting the satisfaction subdomain of the Michigan Hand Outcomes Questionnaire in the matched collagenase injection and limited fasciectomy groups at baseline and at follow-up.



**Fig. 6.** Degree of contracture for metacarpophalangeal (left) and proximal interphalangeal (right) joints affected by recurrent disease in the matched collagenase injection and limited fasciectomy groups at baseline and at follow-up. Least-square means and standard errors from a repeated measures model are plotted. MP, metacarpophalangeal; PIP, proximal interphalangeal.

technique separately, meaningful comparisons have proven to be challenging because of the heterogeneity of their study samples and the wide

variety of endpoints used.<sup>21–24</sup> Although there is some evidence suggesting that better original contracture corrections correspond to a lower risk of

developing recurrence,<sup>25–27</sup> a comparison of the two techniques in terms of recurrence and revision rates is urgently needed to provide patients and providers with more nuanced information required to improve clinical decision-making.

Finally, we acknowledge the inherent drawbacks of propensity score analyses. For example, our matching procedure accounted for imbalance in observed variables only, whereas randomization, when properly conducted, would also account for the differences in possible hidden confounding factors, such as the patient's genetic constitution. It also resulted in the exclusion of a sizable proportion of subjects with comparatively more advanced proximal interphalangeal joint contractures in the limited fasciectomy group, to whom the results of this study do not apply.

## CONCLUSIONS

Considered together, the findings of the present study suggest that collagenase clostridium histolyticum offers an alternative to limited fasciectomy for subjects with metacarpophalangeal joint contractures and those with affected proximal interphalangeal joints who are willing to trade slightly better contracture correction for faster recovery of hand function and a lower risk of serious adverse events. Besides an evaluation of treatments, this study highlights the use of propensity score matching methods for making inferences on the effectiveness of treatments for Dupuytren's disease in actual clinical practice. Future head-to-head studies are required to delineate the long-term effectiveness of collagenase clostridium histolyticum and the established surgical techniques, particularly for those subjects with multiple finger involvement and advanced proximal interphalangeal contractures.

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## ACKNOWLEDGMENT

*The authors thank Nick Hart for contributing to the collection of data.*

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