HANDSURGERY

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Factors predicting the 1-year outcome of collagenase treatment for Dupuytren's disease

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Abstract

Introduction Several studies have investigated the clinical outcome after collagenase treatment for Dupuytren's disease in terms of range of motion of the affected finger. However, good objective clinical outcome defined by a small remaining flexion contracture does not necessarily translate into satisfactory patient-subjective hand function. The aim of the present study was to identify predictors of patient-reported as well as objective clinical outcome in patients 1 year after collagenase treatment for Dupuytren's disease.

Materials and methods Socio-demographic and disease-related data of 92 Dupuytren patients were collected prior to the intervention. Flexion contracture of the most affected finger was measured at baseline and 1 year after treatment. Patients also completed the brief Michigan Hand Outcomes Questionnaire (brief MHQ) before the intervention and at 1-year follow-up. First, univariate correlations using Pearson's correlation coefficient of the baseline variables with the two target variables were investigated. All variables with $r > 0.35$ were selected for a multivariate linear stepwise backwards regression model.

Results The mean brief MHQ score increased between baseline (72 ± 14) and the 1-year follow-up (85 ± 15) ($p \leq 0.001$) and baseline flexion contracture decreased from 76° (± 26) to 33° (± 31) ($p \leq 0.001$). Higher hand function at baseline ($R^2 = 0.31$) and less flexion contracture ($R^2 = 0.46$) were identified as positive predictors for the outcome 1 year after collagenase treatment for Dupuytren's disease. Other variables such as age, gender, manual work and if the MCP or PIP joint was affected did not determine outcome in our patient series.

Conclusions Collagenase treatment resulted in considerable improvement in flexion contracture as well as patient-reported hand function at the 1-year follow-up. Clinicians can expect better outcome after collagenase infiltration in patients with less flexion contracture and in patients showing good initial self-reported hand function.

Keywords Dupuytren's disease · Collagenase *Clostridium histolyticum* · Outcome · Predictive factor

Introduction

Dupuytren's disease (DD) is a proliferative disorder of the palmar fascia causing progressive flexion contracture of the fingers. Severe deformities can lead to loss of hand function, which impairs activities of daily living [1]. Minimally invasive treatment options including the use of collagenase

Clostridium histolyticum (collagenase) are increasingly popular in the treatment of DD [2–9]. This technique effectively reduces contractures and has a lower complication rate in older patients or those with comorbidities when compared to surgical procedures [5, 8, 10]. Surgeons with a greater number of years in practice tend to recommend collagenase treatment more frequently [11].

Several studies report more beneficial effects of collagenase treatment in the early stages of the disease, and treatment of the metacarpophalangeal (MCP) rather than proximal interphalangeal (PIP) joint results in better range of motion of the affected finger [4, 6, 7]. However, good clinical outcome in terms of a small remaining flexion contracture does not necessarily translate into satisfactory patient-subjective hand function [12, 13]. The collection of patient satisfaction data is now more commonly associated with

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the evaluation of surgical care quality [14]. Engstrand et al. showed that the improvement in patient-reported outcome [i.e. Disability of the Arm, Shoulder and Hand (DASH) Questionnaire] after fasciectomy was positively associated with improved range of motion [15]. Zhou et al. revealed higher patient satisfaction after limited fasciectomy for patients with greater self-reported preoperative hand appearance [i.e., Michigan Hand Outcomes Questionnaire (MHQ) subscore] [16]. Similarly, Warwick et al. assessed patient satisfaction after collagenase treatment and found that 73% of patients were very satisfied, although this decreased over time as the disease recurred [17]. Scherman et al., on the other hand, found no difference in the 1-year subjective outcome for DD patients treated with either collagenase injection or needle fasciotomy [18]. To date, there is little information on patient-reported outcomes and the predictive factors for patient-subjective hand function as well as objective clinical outcome after collagenase treatment.

A lack of consistency in the treatment recommendations for patients with DD has recently been recognised [11]. None of the available treatment options is completely curative and each of them is associated with considerable risks. To attain evidence-based agreement regarding treatment recommendations, further investigation of outcome of the current treatment options is needed. An optimal treatment strategy aims at patient-centred care and shared decision-making [19]. Therefore, patient-reported hand functionality as well as clinical outcomes should be considered in decision-making.

The scope of our present study was to identify preoperative factors that determine patient-subjective hand function as well as the range of motion 1 year after collagenase treatment for DD.

Methods

Study design and patient population

This study is based on data from our prospective registry including all patients treated in any form for DD since September 2012. The registry contains a comprehensive assessment of patients prior to treatment (baseline) and 1 year after the intervention. For this specific analysis, we included patients who received a collagenase injection and completed the 1-year follow-up until December 2016. Written informed consent was obtained from every patient prior to inclusion.

Collagenase treatment was carried out by experienced hand surgeons at our clinic. The collagenase injection and subsequent finger extension procedure were performed under local anaesthesia. A single injection of 0.58 mg collagenase [in 0.25 ml diluent (0.03% calcium chloride dihydrate/0.9% sodium chloride) for MCP joints

and 0.20 ml for PIP joints] was applied into the cord of each treated joint. Twenty-four hours after injection, the hand surgeon carried out the finger extension procedure. Every patient received a customised splint for night-time wear (Fig. 1) during a 6-week post-intervention period as well as instructions for undertaking self-mobilization exercises including returning to normal activities as soon as possible.

Assessments

Baseline assessment and 1-year follow-up data were analysed for this study. Prior to the intervention, the following socio-demographic and disease-related data were collected: gender; age; occupation before intervention as well as the degree of associated manual labour; previous alcohol use; diabetes mellitus as a comorbidity; treated finger; recurrent treatment (patients who had previously received at least one treatment for DD); and duration of disease. At baseline and follow-up, range of motion was measured using a standard two-armed finger goniometer. Total flexion contracture was calculated using the sum of flexion contracture for all three finger joints, regardless of whether all joints were treated or not [20]. If more than one finger was affected, data from the finger with the most severe flexion contracture were reported. All patients completed the brief MHQ, which contains twelve items concerning hand function, activities of daily living, pain, work performance, patient satisfaction, and aesthetics [21, 22]. The total summary score lies between 0 and 100 with higher scores indicating better hand function. The brief MHQ shows good measurement properties in patients with different hand disorders including those with DD [21, 23].

Fig. 1 Customized night splint

Statistical analysis

Registry data were managed using the REDCap Electronic Data Capture system and exported for statistical analysis using the Stata 13 software (StataCorp LLC, College Station, TX, USA). Baseline patient demographic and disease-related parameters were tabulated separately using standard descriptive statistics. We investigated the treatment outcome using paired t tests to detect differences between baseline and follow-up brief MHQ scores and flexion contracture.

For our prediction model, we analyzed the effect of baseline factors (i.e., age, gender, affected PIP or MCP joint, brief MHQ score, and flexion contracture) on the brief MHQ score and flexion contracture at 1 year; the prediction model analysis included at least ten patients. Univariate analyses based on the Pearson correlation coefficient (r) of baseline variables with the two target variables were initially made. All variables with, at least, a moderate correlation of $r > 0.35$ were selected for inclusion into a multivariable linear regression model with backwards selection [24]. Furthermore, we added the following variables into the multivariable model based on their clinical relevance: brief MHQ score, flexion contracture, affected MCP, or PIP joint.

Results

Our study sample included a total of 92 patients with a mean age of 67 years and 114 affected fingers (Table 1). The mean brief MHQ score significantly increased between baseline (72 points $\pm$ 14) and the 1-year follow-up (85 points $\pm$ 15) ($p \leq 0.001$). In addition, there was a significant decrease in the baseline flexion contracture by the 1-year follow-up (76° ($\pm$ 26) vs. 33° ($\pm$ 31), $p \leq 0.001$).

The brief MHQ at 1 year only correlated with the brief MHQ at baseline ($r = 0.56$; $p \leq 0001$; Table 2), whereas the flexion contracture at 1 year was only correlated with the contracture at baseline ($r = 0.61$; $p \leq 0001$; Table 3). These variables were entered into two multivariable models. Based on clinical relevance, the brief MHQ and flexion contracture as well as if the MCP or PIP joint was affected were also included.

The multivariate regression analysis showed that only the baseline brief MHQ score determined the brief MHQ score at 1 year ($R^2 = 0.31$, Fig. 2). Flexion contracture at 1 year was only determined by the degree of flexion contracture at baseline ($R^2 = 0.46$) (Table 4, Fig. 3).

Discussion

This study focused on identifying predictors for patient-reported and objective outcome 1 year after collagenase treatment for DD. In summary, patient-reported outcome as

Table 1 Baseline epidemiological and disease-related data of 92 patients

Characteristic	n (%)	Mean (SD)
Age (years)		67 (8)
Gender, male	76 (83)	
Affected finger	114	
Thumb	1 (1)	
Index	1 (1)	
Middle	2 (2)	
Ring	22 (19)	
Little	47 (41)	
More than 1 finger	41 (36)	
Affected joint		
MCP	34 (37)	
PIP	21 (23)	
More than 1 joint	37 (40)	
Brief MHQ score		72 (14)
Flexion contracture (°)		76 (26)
Duration of disease (years)		8.0 (6.9)

n number, *SD* standard deviation, *MCP* metacarpophalangeal, *PIP* proximal interphalangeal, *brief MHQ* brief Michigan Hand Outcomes Questionnaire (total score ranges from 0–100, where 100 indicates better hand performance)

Table 2 Pearson's correlation coefficient (r) between the brief MHQ at 1-year follow-up and baseline variables

Baseline variable	r	p value
Age	− 0.04	0.74
Sex	0.14	0.19
Affected joint		
MCP	0.12	0.29
PIP	− 0.02	0.85
More than 1 joint	− 0.10	0.37
Brief MHQ score	0.56	≤ 0.001
Flexion contracture	− 0.29	0.01
Manual labour	− 0.18	0.28

MCP metacarpophalangeal, *PIP* proximal interphalangeal, *brief MHQ* brief Michigan Hand Outcomes Questionnaire (total score ranges from 0 to 100, where 100 indicates better hand performance)

well as finger range of motion improved significantly 1 year after collagenase treatment compared to the baseline data of our population. Better hand function at baseline, measured with the brief MHQ, determined increased hand function 1 year after treatment. Similarly, a higher degree of flexion contracture at baseline determined worse range of motion at 1 year. No other baseline variables were able to predict the treatment outcome.

Donald et al. found that preoperative contracture was a significant predictor of complete correction at a mean time of 6.4 months after primary fasciectomy. Other variables

Table 3 Pearson's correlation coefficient (*r*) between flexion contracture at 1-year follow-up and baseline variables

Baseline variable	*r*	*p* value
Age	0.08	0.62
Sex	0.06	0.72
Affected joint		
MCP	−0.25	0.12
PIP	0.07	0.70
More than 1 joint	0.20	0.23
Brief MHQ score	−0.17	0.37
Flexion contracture	0.61	≤0.001
Manual labour	0.06	0.86

MCP metacarpophalangeal, *PIP* proximal interphalangeal, *brief MHQ* brief Michigan Hand Outcomes Questionnaire (total score ranges from 0 to 100, where 100 indicates better hand performance)
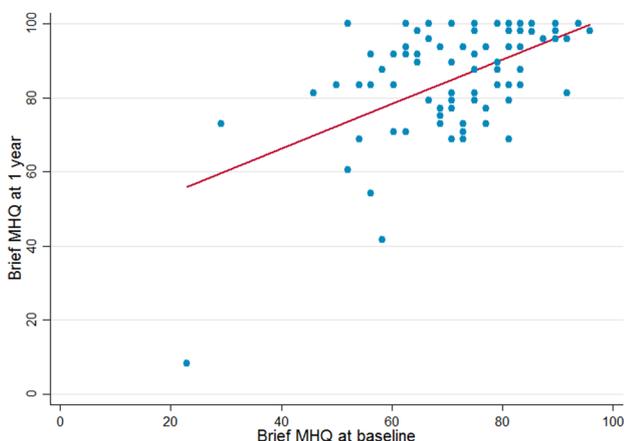

Fig. 2 Relationship between brief Michigan Hand Outcome Questionnaire (MHQ) at baseline vs. 1-year follow-up (beta coefficient = 0.60)

such as age, gender and affected hand or finger did not correlate with the postoperative outcome, which supports our work. Witthaut et al. measured the mean percent change in the degree of contracture and revealed that collagenase injection in patients with less severe MCP and PIP joint contractures had a better clinical outcome compared to

those with severe contractures [7]. Peimer et al. also reported successful treatment (i.e., contracture within 0°–5° of full extension) with collagenase injection in a majority (79%) of patients with less severe contractures before treatment [4]. Based on our findings that a high initial flexion contracture determines a greater contracture at 1 year, we suggest that collagenase treatment for DD patients should be considered primarily when contracture is not yet severe. Advanced contracture may be more successfully treated with surgery [7].

Greater clinical success has been reported for MCP compared to PIP joints through improvement in range of motion [7]. However, neither flexion contracture nor the patient-reported outcomes of our study were significantly correlated with the affected MCP or PIP joint.

All the other variables had no influence on the 1-year outcome after collagenase injection. A high level of exposure to manual work was reported as a risk factor in the development of DD, which led to increased disease severity and was potentially associated with lower treatment success [25, 26]. Nevertheless, we did not find any difference in outcome between patients undertaking greater manual labour to those who do not. Legge and McFarlane observed an increased flexion contracture in the small finger after surgical intervention [27], yet our data show neither an influence of the treated finger on patient-reported outcome nor on flexion contracture after collagenase injection. As the factor of age does not seem to affect results after collagenase treatment, this treatment option provides promising results even for patients at an increased risk for surgical complications. While being female is reported to be associated with better outcome following fasciectomy [28], gender did not predict the outcome after collagenase treatment in our patients.

Several limitations must be noted. First, some characteristics were sparsely distributed in our study population and some data were missing. Second, only one follow-up was assessed. Therefore, we cannot conclude on longer term outcome and unsuccessful outcome at 1-year follow-up may also be caused by recurrent disease. Finally, this study did not include the evaluation of a control group, and therefore, no direct comparisons between collagenase treatment and other treatment modalities can be made.

Table 4 Multivariate models for the brief MHQ and flexion contracture at 1 year

Variable and final model	Coefficient (β)	*p*	95% Confidence interval	R^2
Brief MHQ				0.31
Brief MHQ score at baseline	0.60	≤0.001	0.39–0.81	
Flexion contracture				0.46
Flexion contracture at baseline	0.87	≤0.001	0.51–1.23	

brief MHQ brief Michigan Hand Outcomes Questionnaire (total score ranges from 0 to 100, where 100 indicates better hand performance), R^2 coefficient of determination
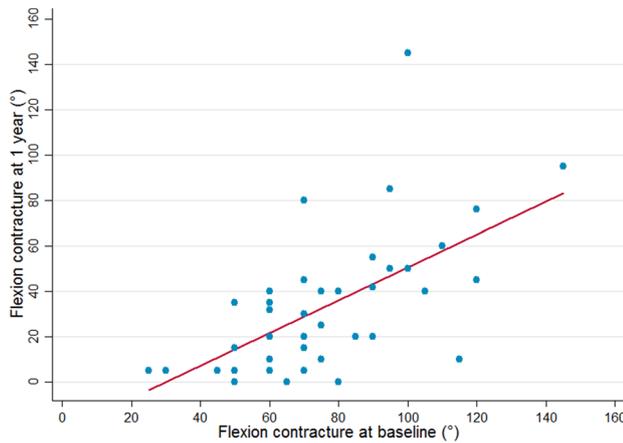
Fig. 3 Relationship between flexion contracture at baseline vs. 1-year follow-up (beta coefficient = 0.87)

To conclude, collagenase treatment for DD resulted in considerable improvement in flexion contracture as well as patient-reported hand function 1 year after injection. Better outcome can be expected after collagenase infiltration in patients with less initial flexion contracture and better initial hand function. Age, gender, manual work and if the MCP or PIP joint was affected did not affect the outcome in our patients.

Compliance with ethical standards

Conflict of interest M. Calcagni has received sponsoring from SOBI for an event on Dupuytren treatment. All other authors have no conflict of interest to declare.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Patient informed consent was obtained from all individual participants included in the study.

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