The risk of skin tear in Dupuytren's disease when treated with collagenase

Christian Fagernæs & Susanne Mallet

ABSTRACT

INTRODUCTION: The purpose of this study was to explore if there was a correlation between joint level and degree of contracture on the one hand and the risk of skin tear in Dupuytren's disease (DD) on the other, when treated with collagenase from *Clostridium histolyticum*. No trial or study has explored the risk of skin tear as primary outcome in a population that has not been treated for DD before.

METHODS: A retrospective study of prospectively collected data was performed on patients with DD treated with collagenase from 1 August 2012 to 1 April 2014. Skin tear was classified as "Yes" or "No" and not quantified by tear size for further analysis.

RESULTS: A total of 105 contractures in 90 patients with DD were included. In all, 77 contractures at the metacarpophalangeal (MP) joint and 28 at the proximal interphalangeal joint (PIP) joint. A total of 59 contractures experienced skin tear. The relative risk (RR) of skin tear was 1.5 for an MP joint of ≥ 60° contracture compared with an MP joint at 20-59° (p = 0.17). The RR of skin tear was 2.2 for a PIP joint of ≥ 60° contracture compared to a PIP joint of 20-59° (p = 0.04). The RR for skin tear was 1.1 for an MP joint compared with the PIP joint (p = 0.74).

The RR for skin tear was 1.7 for contractures of ≥ 60° compared to 20-59° regardless of level (p = 0.01).

CONCLUSIONS: There is a significantly higher relative risk of skin tear when the contracture is ≥ 60° and when the contracture is ≥ 60° and located at the PIP joint. The most important factor regarding the risk of skin tear is the degree of the contracture.

FUNDING: none.

TRIAL REGISTRATION: approved by the Danish Data Protection Agency.

Dupuytren's disease (DD) is a common illness affecting the palmar fascia of the hand causing potentially debilitating contractures of the hand. Several different treatments are available; among these is injection of collagenase from *Clostridium histolyticum*. The physician injects collagenase into the affected Dupuytren's cord. The following day, the contracture is manipulated to achieve rupture of the cord; thereby correcting the contracture [1]. Some trials have explored the treatment of DD with collagenase injection followed by manual manipulation and reported an improved outcome [2-6]. The adverse event (AE) of skin tear is well known and mentioned in most studies [7-9]. To date, however, no study has investigated the risk of skin tear as a primary outcome when treating DD with collagenase and manual manipulation. One study has described the AE of skin tear in 11% of all treated contractures, and another reported 18% skin tear [10, 11]. We wanted to investigate if there was a higher risk of skin tear when the initial contracture was severe.

The aim of this study was to explore the connection between an affected joint and its degree of contracture relative to the likelihood of skin tear when manually manipulated the day after collagenase injection. The objectives were to determine the following: i) does severe contractures carry a higher risk of skin tear than less severe contractures, and ii) are there differences between the risk of skin tear according to level, i.e. metacarpophalangeal joint (MP), proximal interphalangeal joint (PIP) and distal interphalangeal joint (DIP)?

METHODS

Design

This was a retrospective study based on prospectively collected data. All patients with DD who were treated with collagenase from 1 August 2012 to 1 April 2014 in our clinic met the inclusion criteria and were enrolled in the study.

Contractures were measured before and after treatment, and any skin tear was noted in the patient's files. Patients with skin tear were followed until total wound healing.

All patients were examined, treated and followed by a single physician. Relevant data were entered into a database (Excel) and extracted from the database for further analysis to meet the aims and purpose of the study.

Patients

Patients referred by their physician to the orthopaedic department from 1 August 2012 to 1 April 2014 were enrolled in the study if they met the inclusion criteria. Eligible patients were ≥ 18 years old, had not previously been treated for DD on the specific finger, had a palpable cord on clinical exam, had a joint contracture ≥ 20° for either the MP joint or the PIP joint and had given

ORIGINAL ARTICLE

Orthopaedics, Zealand University Hospital, Køge, Denmark

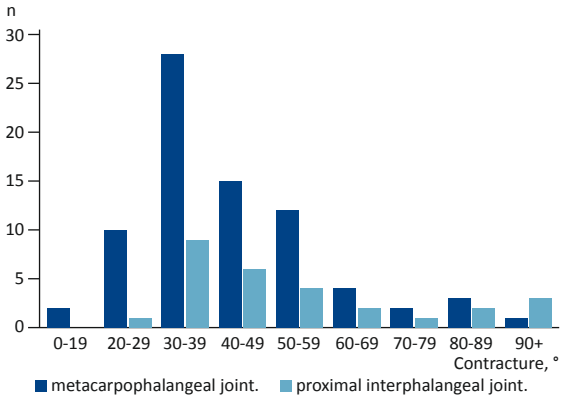
Dan Med J 2018;65(5):A5478

FIGURE 1

An adverse event in the form of skin tear after manipulation on day two.

FIGURE 2

Distribution of cases in groups of contracture.



their written consent. The exclusion criteria were allergies to collagenase or other contents in the product used, coagulation disease, ongoing treatment with tetracyclines, fluoroquinolone or anticoagulant medicine that could not be paused for five days, wounds on the specific finger, receiving other clinical trial medicine or former nerve or skin lesions on the specific finger. No patients were excluded. We chose to divide the degree of contracture into two groups when comparing the risk of skin tear. One group included contractures of 20-59°, and the other included contractures of ≥ 60°.

Technique

The treatment was performed in the course of two days. On day one, the passive degree of contracture was measured, and the physician's case report form was initiated. The measurement was done using a goniometer, and 0.58 mg collagenase was injected 0.5 cm proximally to the distal palmar crease if the contracture was at the MP joint and 0.58 mg was injected 0.5 cm distally to the palmar digital crease if the contracture was at the PIP joint. 0.58 mg collagenase was injected into the cord on both joint levels, as this is the recommended dose when treating Dupuytren's contractures with collagenase [1]. Patients were instructed to keep the treated hand elevated and at rest until the next day, and they were asked not to manipulate the finger themselves. They were told to take painkillers in case of pain.

On day two, the specific finger was injected with 4-5 ml lidocain 2% in the area of the first injection. After 20 minutes, the physician manipulated the finger to attempt rupture of the cord. After manipulation, the remaining passive degree of contracture was recorded in the case report form, as was the event of skin tear, if present. One consultant orthopaedic surgeon did the injection, manipulation and measurement in accordance with the guidelines. If the patient experienced skin tear, the tear was treated in accordance with the guidelines for wound treatment and the patient was seen at extra follow-ups by a designated specially trained nurse, accompanied by the consultant surgeon, until the wound had totally healed. All patients were seen at a three-month follow-up.

Assessment

The consultant orthopaedic surgeon used a goniometer to measure the degree of contracture before and after the manual manipulation. The degree of contracture and the joint level of contracture were recorded in the physician's case report form. Skin tear was recorded as present or not and not, quantified by tear size. A goniometer was also used at the three-month follow-up and data were entered in the case report form. The same consultant orthopaedic surgeon did all the measurements. Data were transferred to a database in Excel for analysis.

Statistics

Fisher's exact test and the chi-squared test were used when calculating the RR and p-values. An independent statistician from The University of Copenhagen, Denmark, calculated the statistics.

Trial registration: The study was approved by The Danish Data Protection Agency.

RESULTS

Overall

A total of 90 patients were enrolled. Seven patients were represented twice, and four patients were represented three times; thus, a total of 105 contractures in 90 patients were included in the study. No patient received the treatment twice in the same finger.

There were 88 (84%) contractures in males (the median age was 67 years) and 17 (16%) contractures in females (the median age was 68 years). Of the entire group, 59 (56%) contractures experienced skin tear when manipulated on day two. **Figure 1** shows an example of skin tear.

We found 77 (73%) contractures with the contracted cord at the MP joint and 28 (27%) contractures at the PIP joint. No patient had the contracted cord at the level of the DIP joint.

The distribution of contractures in different groups of degree is shown in **Figure 2**.

Distribution

A total of 67 contractures were found at the MP joint with a degree of contracture between 20° and 59°, and 36 (54%) of those experienced skin tear. Ten contractures were found at the MP joint with a contracture ≥ 60° and eight (80%) of those experienced skin tear. The distribution is shown in **Table 1**.

We found 20 contractures at the PIP joint with a contracture between 20° and 59° and eight (40%) of those experienced skin tear. Eight contractures were found at the PIP joint with a contracture ≥ 60° and seven (88%) of those experienced skin tear. The distribution is shown in Table 1.

Statistics

For our first objective, the RR for skin tear was 1.7 (p = 0.01) for contractures ≥ 60° compared with 20-59° regardless of joint level. For our secondary objective, the RR of skin tear was 1.5 for the MP joint of ≥ 60° contracture compared with the MP joint at 20-59° (p = 0.17). The RR of skin tear was 2.2 for the PIP joint of ≥ 60° contracture compared with the PIP joint at 20-59° (p = 0.04). The RR for skin tear was 1.1 (p = 0.74) for the MP joint compared with the PIP joint. The statistics are shown in Table 1.

TABLE 1

Distribution of level of contracture, degree and relative risk from compared groups.

	No skin tear, n	Skin tear, n (%)	Total, n (%)	RR of skin lesion	p-value
Level					
MP:					
20°-59°	31	36 (54)	67 (64)	-	-
≥ 60°	2	8 (80)	10 (10)	-	-
Subtotal	33	44 (57)	77 (73)	-	-
PIP:					
20°-59°	12	8 (40)	20 (19)	-	-
≥ 60°	1	7 (88)	8 (8)	-	-
Subtotal	13	15 (54)	28 (27)	-	-
All	46	59 (56)	105 (100)	-	-
Characteristic					
MP, ≥ 60° vs 20°-59°	-	-	-	1.5	0.17
PIP, ≥ 60° vs 20°-59°	-	-	-	2.2	0.04
MP vs PIP, all degrees	-	-	-	1.1	0.74
≥ 60° vs 20°-59°, all levels	-	-	-	1.7	0.01

MP = metacarpophalangeal joint; PIP = proximal interphalangeal joint; RR = relative risk.

DISCUSSION

In this study, we found an association between the joint level and the degree of contracture and the risk of skin tear.

This finding can be used to inform patients considering collagenase treatment. Patients with severe contractures could consider other treatment modalities. We found no post procedure infections among patients with skin tears. Although a skin tear could be perceived as a coarse AE to the patient, it is our opinion that it is but a minor AE with minor long-term risks. Our results showed a higher number of skin tears compared with previous studies [11]. An explanation could be that our manual manipulation technique is less considerate than that of other physicians. However, none of the previous studies at hand were comparable as they describe DD in the thumb or treatment of more than one cord [7].

We are confident that our results are representative as we have tried to minimise the influence of external bias by excluding tissue softeners of any kind used to reduce the risk of skin tear before manipulation. Limitations of the study include that we subdivided the degrees of contracture into the two groups prior to the demographic findings. This subdivision turned out to be rather arbitrary and could have comprised another group including for example 35-50° of contracture. This group of patients has functional difficulties and is therefore more likely to seek treatment for DD than patients with a minor contracture. A subdivision into three groups might have shown an even higher risk of skin tear in patients with a severe contracture compared with patients with a minor contracture. Another limitation is that we did not stratify for co-morbidities, alcohol consumption or smoking habits. We did not record the size of skin tear or actual duration of wound healing in patients with skin tear. No records were kept to establish if or for how long the skin tears kept patients from

returning to their normal occupation. The patients with skin tear were seen the day after treatment by a designated nurse in the outpatient clinic and again 2-3 times more until healing. The mean time that patients with skin tear were unable to attend their job was assumed to be about two weeks, but we have no record of the actual time span. This is an important point if one wishes to analyse the cost-benefit of the treatment in future studies.

The strength of the study was that a single consultant orthopaedic surgeon carried out the measurement and treatment of the contractures making the treatment and measurements consistent. However, we do not know if the treatment is representative of the standard treatment done by other orthopaedic surgeons with respect to the actual injection point of collagenase and the manual technique used to attempt rupture on day two.

It is our belief that even though skin tear occurs, treatment with collagenase in Dupuytren's contracture is more considerate, less invasive and overall less costly than open surgery.

CONCLUSIONS

In collagenase treatment of Dupuytren's contracture, we found a significantly higher relative risk of skin tear in joint contracture exceeding 60°, and the highest risk in contractures exceeding 60° and located at the PIP joint.

We found the risk of skin tear to be independent of joint level.

Therefore, focus is needed on patients with a contracture exceeding 60°. Further investigation is warranted to determine if a kind of tissue softener, different manual manipulation technics or e.g. a time span of two days before manipulation may decrease the risk of skin tear when treating Dupuytren's contracture with collagenase. Also, a cost-benefit comparison of collagenase treatment versus open surgery is relevant.

CORRESPONDENCE: *Christian Fagernæs.*
E-mail: christianbenned@gmail.com

ACCEPTED: 28 February 2018

CONFLICTS OF INTEREST: none. Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

LITERATURE

1. Annex I. Summary of product characteristics. European Medicines Agency, 2011. www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002048/WC500103373.pdf (9 Jan 2018).
2. Coleman S, Gilpin D, Kaplan FT et al. Efficacy and safety of concurrent collagenase Clostridium histolyticum injections for multiple Dupuytren contractures. J Hand Surg Am 2014;39:57-64.
3. Eaton C. Evidence-based medicine: Dupuytren contracture. Plast Reconstr Surg 2014;133:1241-51.
4. Hallock GG. Skin laceration as a serious adverse sequela of injectable collagenase for Dupuytren contracture. Plast Reconstr Surg 2012;129: 205e-206e.
5. Knobloch K, Vogt PM. Beware of the small finger and/or the proximal interphalangeal joint. Skin lacerations following collagenase injection in Dupuytren contracture. Plast Reconstr Surg 2012;130:202e-204e.
6. Nydick JA, Olliff BW, Garcia MJ et al. A comparison of percutaneous needle fasciotomy and collagenase injection for Dupuytren disease. J Hand Surg Am 2013;38:2377-80.
7. Bendon CL, Giele HP. Collagenase for Dupuytren's disease of the thumb. J Bone Joint Surg Br 2012;94:1390-2.
8. Spanholtz TA, Holzbach T, Wallmichrath J et al. Treatment of Dupuytren's contracture by means of injectable collagenase: first clinical experiences. Handchir Mikrochir Plast Chir 2011;43:275-80.
9. Considine S, Heaney R, Hirpara KM. Early results of the use of collagenase in the treatment of Dupuytren's contracture. Ir J Med Sci 2015;184:323.
10. Lawrence C, Hurst, MD, Marie A et al. Injectable collagenase Clostridium histolyticum for Dupuytren's contracture. N Engl J Med 2009;361:968-79.
11. Manning CJ, Delaney R, Hayton MJ. Efficacy and tolerability of day 2 manipulation and local anaesthesia after collagenase injection in patients with Dupuytren's contracture. J Hand Surg Eur 2014;39:466-71.