

INTRODUCTION:

Collagenase has been investigated in phase II and ongoing phase III clinical trials for the treatment of Dupuytren's disease. The purpose of this study is to establish long-term results in a subset of patients who underwent collagenase injection for the treatment of Dupuytren's contracture.

METHODS:

The 23 patients who had participated in the Phase II clinical trial of injectable collagenase at Stanford University Medical Center in 1999-2000, were contacted by letter and phone. 9 subjects were available for follow-up examination. One patient had received placebo injection and was excluded. The remaining 8 patients completed a Dupuytren's Disease questionnaire and underwent independent examination of joint motion by a single examiner.

RESULTS:

Eight patients participated in the 8-year follow-up study: 6 had been treated for isolated MCP joint contracture, 2 patients had been treated for isolated PIP joint contracture.

Average pre-injection contracture was 57.2° in the MCP group. Average contracture was 8.8° at 1 week, 10.8° at 1 year and 22.5° at 8 year follow-up. 67% (4/6) patients experienced recurrence while 33% (2/6) had no evidence of disease recurrence at 8-year follow-up. No patients had undergone further intervention on the treated finger.

Average pre-injection contracture was 45° in the PIP group. Average contracture was 7.5° at 1 week, 15° at 1 year and 60° at 8 year follow-up. 100% (2/2) patients experienced recurrence. No patients had undergone further intervention on the treated finger.

Patients subjectively rated the overall clinical success at 60% (range 0 to 100%) and 87.5% of patients stated that they would pursue further injection for the treatment of recurrent or progressive disease.

SUMMARY POINTS:

- Enzymatic fasciotomy is safe and efficacious with initial response to injection resulting in reduction of joint contracture to within 0 to 5° of normal in 90% of patients.
- Long-term recurrence rates suggest recurrence in 67% of MCP joint contractures and 100% of PIP joint contractures; however, recurrence was generally less severe than the initial contracture.
- Patient satisfaction is high with 87.5% of patients stating that they would pursue further injection for treatment of recurrent or progressive disease.
- These data support a role for collagenase injection in the treatment of Dupuytren's contracture, particularly in patients with isolated MCP joint contractures and those who are reluctant to proceed with surgical intervention or minimize recovery time.

REFERENCES:

1. Badalamente MA, Hurst LC, Hentz VR. Collagen as a Clinical Target: Nonoperative Treatment of Dupuytren's Disease. *J Hand Surg* 2002; 27A: 788-798.
2. Badalamente MA, Hurst LC. Efficacy and Safety of Injectable Mixed Collagenase Subtypes in the Treatment of Dupuytren's Contracture. *J Hand Surg* 2007; 32A: 767-774.
3. Badalamente MA, Hurst LC. Enzyme Injection as Nonsurgical Treatment of Dupuytren's Disease. *J Hand Surg* 2000; 25A:629-636.
4. Shaw RB, Chong AKS, et al. Dupuytren's Disease: History, Diagnosis, and Treatment. *J Plast Reconstr Surg* 2007; 120(3): 44-54.

- ▲ Presentation will discuss Collagenase by Auxilium
- Research or institutional support received from Auxilium; funding for ongoing phase III clinical trial of Collagenase

HS-Paper 17

Friday, September 4, 2009 * 10:12-10:19 AM
Clinical Paper Session 4: Dupuytren's

Dupuytren's Disease and Fibroblast Contractility

Level I Evidence

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HYPOTHESIS:

Myofibroblasts (which express $f\zeta$ -smooth muscle actin ($f\zeta$ -SMA)) within Dupuytren nodules are putatively responsible for disease progression; however, previous study showed these cells are often only focally present and in certain instances may be absent. In contrast, fibroblasts are diffusely present in Dupuytren nodules and in vitro work demonstrates that fibroblasts remodel their extracellular matrix through actomyosin contractility. It is hypothesized that both fibroblasts and myofibroblasts cause Dupuytren contractures and the contractile proteins non muscle myosin IIA and IIB (NMMIIA and NMMIIB) are robustly expressed in both these cells. The important question is not which cell causes Dupuytren contractures, because fibroblasts and myofibroblasts are similar, but rather what are the intracellular proteins that mediate cell contractility to cause contractures.

METHODS:

Tissues from Dupuytren fascia (n=10) and normal palmar fascia (n=10) were immunostained for $f\zeta$ -SMA, NMMIIA, and NMMIIB, and sections were analyzed with the assistance of a Dermatopathologist.

RESULTS:

The cellular areas arranged in nodules had plump nuclei and robustly expressed NMMIIA and NMMIIB, in comparison to quiescent appearing cords and normal palmar fascia. NMMIIA and NMMIIB were ubiquitously expressed throughout nodules whereas $f\zeta$ -SMA was focally absent.

SUMMARY POINTS:

The notion that myofibroblasts cause Dupuytren's disease may be incomplete. Immunohistochemical analysis demonstrates that NMMII isoforms are expressed throughout nodules but myofibroblasts are not. The relative expression pattern of $f\zeta$ -SMA, in conjunction with the ubiquitous expression of NMMII in nodule fibroblasts but not normal palmar fascia or Dupuytren cords, would suggest both fibroblasts and myofibroblasts play a role in Dupuytren contractures. Prevention of myofibroblast

formation may be insufficient to prevent Dupuytren's disease; rather, inhibition of the common contractile proteins NMMIIA and NMMIIB in both fibroblasts and myofibroblasts may be necessary to prevent Dupuytren's disease progression.

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HS-Paper 18

Friday, September 4, 2009 * 10:19-10:26 AM
Clinical Paper Session 4: Dupuytren's

An Anatomic and Biomechanical Study of Landsmeer's Oblique Retinacular Ligament and its Role in Finger Extension

Level I Evidence

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HYPOTHESIS:

The oblique retinacular ligament (ORL) is a constant anatomic structure and assists in distal interphalangeal (DIP) joint extension when the proximal interphalangeal (PIP) joint is extended.

METHODS:

40 fresh frozen fingers were used for this study and the presence and consistency of the ORL was noted. The fingers were mounted in a custom designed jig that allowed full motion at the MP and IP joints. The distal phalanx was connected to an Instron 5848 which allowed precisely calibrated DIP flexion with the ability to measure the force required to flex the joint in varying PIP and MP positions. The force required to flex the DIP joint was then assessed with the PIP joint in 0, 30, 60 and 90 degrees of flexion, as well as varying the MP joint positions of 0 and 45 degrees. The 'normal' force was measured and then all measurements were repeated following serial sectioning of the ORL, and subsequently the central slip.

RESULTS:

The ORL was present on the radial and ulnar sides of each finger in 38 specimens. The ORL tended to be more robust in the ring finger followed by the index, middle and small fingers, respectively.

In the intact finger DIP flexion force was greatest at 30 degrees of PIP flexion and least at 90 degrees of PIP flexion. There was statistical significance between the 90 degree and all other positions of PIP flexion with respect to flexion force in the intact specimen.

Serial sectioning of the ORL revealed that it contributed 25% to the total force required to flex the DIP joint with the PIP at 0 degrees, 31% at 30 degrees ($p < .001$), 18% at 60 degrees, and 3% at 90 degrees. MP joint position of 0 or 45 degrees did not affect the force required to flex the DIP joint.

Sectioning the central slip revealed a statistically significant effect at 90 degrees of PIP flexion where the force required to flex the DIP joint increased by 77%.

SUMMARY POINTS:

- The ORL is a relatively constant anatomic structure most robust in the ring and index fingers, and least robust in the small finger.
- The ORL contributes approximately 25 to 30% of the resistance to DIP flexion with the PIP at 0 to 30 degrees of flexion and a minimal amount at 90 degrees of flexion.
- The intact central slip accounts for the decrease DIP flexion force at 90 degrees PIP flexion.

HS-Paper 19

Friday, September 4, 2009 * 10:26-10:33 AM
Clinical Paper Session 4: Dupuytren's

Anatomy of Irreducible Metacarpophalangeal Joint Dislocation in a Cadaver Model

Level of Evidence Not Applicable

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HYPOTHESIS:

Considerable controversy exists over the anatomy of irreducible dorsal metacarpophalangeal dislocation. The aim of this work is to a: develop a cadaveric model of MP dislocation that closely simulates the clinical situation, and b: study the anatomy of the structures around the MP joint and their contribution to irreducibility of the dislocation. We hypothesize that 1) the flexor tendons, lumbricals and the superficial transverse and natatory ligaments (Kaplan's original "noose" theory) do not cause the irreducibility, and 2) division of the volar plate is necessary to reduce the dislocation.

METHODS:

Nine fresh cadaveric hands were used in this study. The hands were amputated just proximal to the carpus and stabilized in a specially formulated fixture. An index finger MP joint dislocation was created by an impact load delivered by a servohydraulic testing machine (MTS Systems), at a displacement rate of 100 mm/s and with a maximum displacement of 60 mm. Closed reduction of the dislocation was attempted, followed in irreducible cases by an open dissection of the joint to identify the anatomy of the structures around the MP joint and the cause of the irreducibility.