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TRANSVERSE CARPAL LIGAMENT ELONGATION AFTER INJECTION OF COLLAGENASE IN SITU

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INTRODUCTION

The transverse carpal ligament (TCL) forms the volar boundary of the carpal tunnel, making it relevant compression neuropathy of the median nerve at the wrist. Although the etiology of carpal tunnel syndrome in unclear, it has been associated with higher carpal tunnel pressure, sometimes reaching above 200mmHg [1]. The current standard treatment for carpal tunnel syndrome is to surgically transect the TCL in order to increase carpal tunnel space and decompress the median nerve. However, this can disrupt the important biomechanical functions of the TCL and result in side effects such as pillar pain or hand weakness [2]. A potential alternative to surgery could be to increase TCL elasticity, allowing it to elongate in response to elevated carpal tunnel pressure. Collagenase Clostridium Histolyticum (CCH) is an enzyme that breaks down collagen fibers and can be injected into the TCL to increase its elasticity. The purpose of this study was to investigate the effects of CCH injections on the elongation of TCL tissue when carpal tunnel pressure is applied.

METHODS

Six fresh-frozen cadaveric hands were used in this study. The carpal tunnel contents were emptied, and a medical balloon connected to a pressure regulator was inserted into the tunnel. 18 retroreflective markers (Φ = 1mm) were attached to the volar surface of the transverse carpal ligament in a 6x3 grid, such that the 3 rows were placed along the distal border, the proximal border, and centered between the proximal and distal border. The six markers in each row were evenly spaced between the radial and ulnar borders of the TCL. Nine evenly spaced injection sites were marked along the TCL midline (Figure 1) using tissue marking dye. Collagenase solution with a concentration of 50U/μL was prepared by dissolving CCH in phosphate buffered saline. Each injection site was injected with 5μL of the solution so that it received 250U of CCH, and the specimen was placed in an incubator set to 37°C.

The specimen was removed from the incubator 24 hours after injection and placed on a table with the wrist in a neutral position. Four Vicon cameras were set up to capture the marker positions (Figure 1). The medical balloon in the carpal tunnel was connected to a pressure regulator using plastic tubing. Using the pressure regulator, the carpal tunnel was inflated to 10, 30, 60, 90, 120, 150, 180, and 210 mmHg. At each pressure level, 3 seconds of video were recorded by the Vicon cameras.

Figure 1: Four Vicon cameras recording marker positions at each pressure level.

The 3D coordinates of each marker at each pressure level were obtained. The injection group for each row consisted of the centermost pairs of markers that contained a CCH injection between them. The control group consisted of all other pairs of markers. Distances between adjacent markers in the same row were calculated using MATLAB. Percent elongation was calculated for each pair of adjacent markers in the same row using the following equation:

$$\%\delta = \frac{d_i - d_{10}}{d_{10}} \quad (1)$$

Where d_{10} is the distance between the markers at the baseline carpal tunnel pressure of 10 mmHg and d_i is the distance between the markers at the i^{th} pressure.

Mean percent elongations of the injection group and control group were calculated for the proximal, middle, and distal rows. Pearson's correlation coefficient and linear regression analysis was used to determine the relationship between pressure and percent elongation for the injection group. Two-way RM ANOVA was performed to determine the effect of pressure and CCH injection on percent elongation. Pairwise comparisons were determined using Tukey's test.

RESULTS

Percent elongations of each group are shown in Figure 3. The proximal, middle, and distal TCL in the injection group had significantly greater elongation than the control group at pressure levels 60 mmHg and above ($p < 0.001$), 60 mmHg and above ($p < 0.001$), and 120 mmHg ($p < 0.002$) and above, respectively. For the injection group, the percent elongations at 210 mmHg for the proximal, middle, and distal rows were 6.3 ± 0.7%, 5.8 ± 1.0%, and 4.9 ± 2.8%, respectively. For the control group, the percent elongations at 210 mmHg for the proximal, middle, and distal rows were 0.4 ± 0.3%, 0.4 ± 0.3%, and 0.5 ± 0.3%, respectively. In some specimens, visible tearing of the TCL occurred at high pressure levels (≥ 180mmHg) where CCH was injected.

In the injection group, Pearson's correlation coefficient showed a strong positive correlation between pressure and percent elongation for the proximal ($r = 0.79$) and moderate positive correlations for the middle ($r = 0.64$), and distal ($r = 0.53$) rows The fitted regression models of the proximal, middle, and distal rows for the injection group were $y = 2.6 \times 10^{-4}x + 0.01$, $y = 2.2 \times 10^{-4}x + 0.02$, and $y = 1.68 \times 10^{-4}x + 6.5 \times 10^{-3}$, respectively. In the control group, weak positive correlations were found for the proximal row ($r = 0.13$), the middle row ($r = 0.23$), and the distal row ($r = 0.07$).

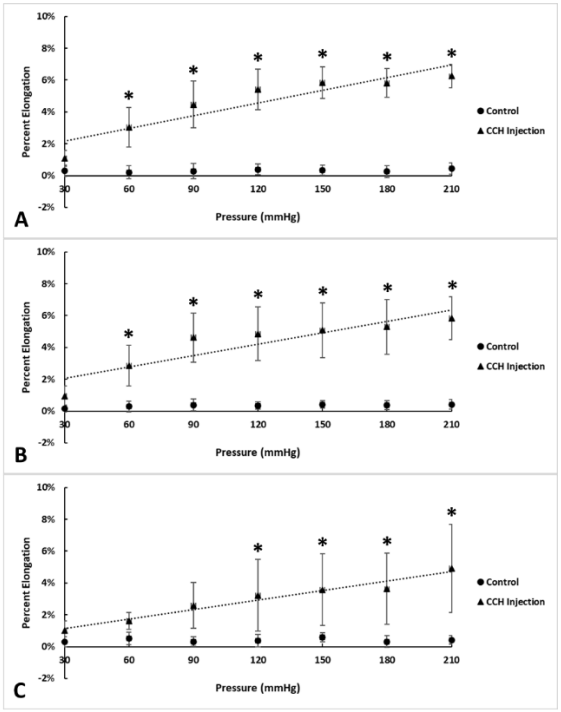

Figure 2: Percent elongation at each pressure level for the proximal (A), middle (B), and distal (C) regions of the TCL.

DISCUSSION

This study investigated the relationship between carpal tunnel pressure and percent elongation of TCL tissue injected with CCH. We found that the intact locations experienced no elongation, while the injection locations experienced significant percent elongation at elevated pressure levels and had a strong positive correlation between pressure and percent elongation.

The proximal, middle, and distal regions of the control group had percent elongations of 0.5%, 0.4%, and 0.5%, respectively, when 210 mmHg of carpal tunnel pressure was applied. These results agree with previous literature that the TCL is relatively unable to be stretched [3]. The proximal, middle, and distal regions of the injection group experienced 6.3%, 5.8%, and 4.9% elongation when 210 mmHg of carpal tunnel pressure was applied. While healthy people can have a carpal tunnel pressure around 2.5 mmHg, those with carpal tunnel syndrome tend to have tunnel pressures above 30 mmHg [1]. When CCH breaks down the collagen fibers in the TCL, the TCL becomes more elastic, allowing it to elongate and yield to carpal tunnel pressure. This elongation also creates more carpal tunnel space, alleviating pressure off the median nerve.

In the injection locations, the distal region of the TCL had lower percent elongations than the proximal and middle regions and required higher carpal tunnel pressure to reach significantly greater percent elongation than the intact locations. Because median nerve compression usually occurs at the distal end of the carpal tunnel [4], elongating the distal region of the TCL would be most important for nerve decompression. Previous studies have found that the TCL tends to be thickest distally in the center [5], which could explain the distal region experiencing less elongation than the middle and proximal regions. To account for this, a higher dose of CCH could be used in the distal region to achieve the same elongation as the proximal and middle regions.

In the injection group, tearing of the TCL occasionally occurred in the middle region when pressures of 180 mmHg or greater were applied. This tearing of the TCL could allow CCH to leak into the carpal tunnel and cause undesired effects to the tunnel contents. Also, tearing could disrupt the biomechanical functions of the TCL, such as providing an anchor for the thenar muscles. A possible solution to this is to decrease the amount of CCH injected to the middle region.

Our results suggest that CCH injection is effective in elongating the surrounding TCL tissue under elevated carpal tunnel pressure. One line of injections was delivered along the TCL midline to achieve these results, but multiple lines of injections could be delivered for greater elongation of the entire TCL. Also, the distal region of the TCL is less affected by CCH injection and may require a higher dose of CCH, while the middle region may require a lower dose to prevent tearing of the tissue. These findings support that CCH injection has potential as a treatment for carpal tunnel syndrome and should be further explored. While we investigated the local effects of CCH injection on TCL tissue, future studies can investigate the effects of CCH injection on total TCL length and carpal arch morphology.

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