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Pathological changes in the subsynovial connective tissue increase with self-reported carpal tunnel syndrome symptoms

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ABSTRACT

Background: Fibrosis and thickening of the subysnovial connective tissue are the most common pathological findings in carpal tunnel syndrome. The relationship between subsynovial connective tissue characteristics and self-reported carpal tunnel syndrome symptoms was assessed.
Methods: Symptoms were characterized using the Boston Carpal Tunnel Questionnaire and Katz hand diagram in twenty-two participants (11 with symptoms, 11 with no symptoms). Using ultrasound, the thickness of the subsynovial connective tissue was measured using a thickness ratio (subsynovial thickness/tendon thickness) and gliding function was assessed using a shear strain index ((Displacement$_{tendon}$ − Displacement$_{subsynovial}$) / Displacement$_{tendon}$x 100). For gliding function, participants performed 10 repeated flexion–extension cycles of the middle finger at a rate of one cycle per second.
Findings: Participants with symptoms had a 38.5% greater thickness ratio and 39.2% greater shear strain index compared to participants without symptoms ($p < 0.05$).
Interpretation: Ultrasound detected differences the SSCT in symptomatic group that was characterized by low self-reported symptom severity scores. This study found ultrasound useful for measuring structural and functional changes in the SSCT that could provide insight in the early pathophysiology associated with carpal tunnel syndrome symptoms.

1. Introduction

Carpal tunnel syndrome (CTS) is the most frequently reported peripheral neuropathy. It is characterized by pain, paresthesia or weakness in regions innervated by the median nerve. The diagnosis of CTS can include a combination of physical examination, patient history for signs and symptoms, and electrodiagnostic tests (nerve conduction studies or needle electromyography). Clinicians frequently use electrodiagnostic tests for objective assessment of the pathophysiology by measuring motor and sensory nerve conduction velocities to determine neurological impairment (reduced velocity indicates damage) (Rempel et al., 1998). However, nerve conduction velocities can be affected by testing parameters such as electrode size, inter-electrode distance, amplifier gain, and tissue temperature (Jordan et al., 2002). Additionally, diagnoses involve comparing conduction velocities to normative values that are not well standardized (Rempel et al., 1998). These factors may account for the variable sensitivity in electrodiagnostic tests, leading to false negatives in the range of 49% to 84%, and suggest the need for additional tests to aid in the diagnosis of CTS (Jordan et al., 2002). With false negatives, an accurate and comprehensive clinical history becomes even more important.

While there is no single best way to assess CTS symptom characteristics, the Boston Carpal Tunnel Questionnaire (BCTQ) and Katz hand diagram are established techniques. The BCTQ is a self-administered survey that provides information on the severity of symptoms and functional status (Levine et al., 1993). It has excellent reproducibility, responsiveness, and internal consistency (Levine et al., 1993). The Katz hand diagram is also useful as it allows patients to visually document the location of symptoms, specifically those that are relevant to the median nerve innervations, with high reproducibility, sensitivity and specificity (Katz and Stirrat, 1990). These tests are pragmatic for clinical practice as they are non-invasive and easily-administered. However, questionnaires alone are inadequate to diagnose CTS since self-reported symptoms could be subjective and do not provide detail on the aetiology of the nerve or surrounding tissue (Jablecki et al., 1993).

Alternatively, ultrasound can be used to examine structures in the carpal tunnel including the median nerve and surrounding tissue. Recent advances in ultrasound resolution have also led to new findings including fibrosis and thickening of the surrounding tissue called the subsynovial connective tissue (SSCT) that have become a common pathological finding in CTS patients (Ettema et al., 2006; van Doesburg et al., 2012a). The SSCT is composed of layers of collagen bundles that

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are interconnected by perpendicular fibres, which mediate motion between the flexor tendons and median nerve. Pathological changes can impair the gliding function of the SSCT resulting in reduced SSCT excursions. Ultrasound-based measurements of SSCT excursions were used in a recent study to predict the most affected hand in CTS patients, resulting in high accuracy rates of 87% (Korstanje et al., 2012). This highlights the diagnostic potential of evaluating the SSCT structure.

Excessive shear force between the SSCT and adjacent structures (tendon and nerve) has been implicated in the development of pathological changes in the SSCT. Large shear forces can stretch the SSCT fibrils beyond their elastic limits and break the interconnections resulting in "shear injury" (Ettema et al., 2008; Vanhees et al., 2012). This shear injury can occur with finger motions that cause significant differential motion between the tendon and SSCT and/or nerve and SSCT. Epidemiological studies are consistent in showing a link between hand and finger motion, especially with high repetition and long duration, and CTS (Moore et al., 1991; Silverstein et al., 1987). While the role of physical work factors has been well investigated, the clinical implications of SSCT fibrosis and thickening are still unclear.

Ultrasound has the ability to detect small morphological and functional changes in the SSCT. This study used ultrasound to evaluate SSCT thickness and SSCT mechanics using a high frequency, repetitive finger task in participants with and without self-reported CTS symptoms. We explored the relationship between SSCT characteristics and severity of CTS symptoms using the BCTQ and Katz hand diagram. We hypothesized that increased SSCT thickness and impaired gliding function in the SSCT would be positively associated with CTS symptom scores. A better understanding of the clinical implications of SSCT fibrosis and thickening may help to elucidate the clinical utility of ultrasound in the assessment of CTS.

2. Methods

2.1. Participants

Twenty-two participants were recruited for this study including eleven participants with self-reported CTS symptoms (9 women and 2 men) with a mean age (standard deviation) of 26.2 (3.1) years and eleven participants without symptoms (9 women and 2 men) with a mean age of 41.5 (13.1) years. Each participant was screened for musculoskeletal disorders of the hand and wrist using an exclusion questionnaire for previous wrist surgery, radial malunion, Colles fracture, bifid median nerve, degenerative joint disease, arthritis of the wrist/hand, gout, hemodialysis, sarcoidosis, amyloidosis, hypothyroidism, and diabetes mellitus. Informed consent was obtained prior to participation. The study was approved by the Hamilton Health Sciences and McMaster Health Sciences Research Ethics Board.

All participants completed the Boston Carpal Tunnel Questionnaire (BCTQ) and Katz Hand diagram to assess CTS symptoms. The BCTQ consists of a symptom severity and a functional status evaluation (Levine et al., 1993). Symptom severity is assessed using multiple choice questions related to classic CTS symptoms (pain, paraesthesia, numbness, weakness, and nocturnal symptoms) on a 5-point scale (0–4 points). Functional status assessed the self-reported level of difficulty in performing daily tasks (writing, buttoning, gripping, opening, bathing, dressing) using the same scoring. The symptom severity and functional status scores were calculated as the mean score reported in each questionnaire. The Katz hand diagram documents the distribution of symptoms (pain, tingling, numbness, decreased sensation) on the hand and forearm scored from 0 to 3 based on the location and type of symptoms relevant to median nerve compression (Katz and Stirrat, 1990). Participants were considered to have CTS symptoms if they reported positively in at least one of the severity questionnaires (BCTQ symptom severity, BCTQ functional status, Katz hand diagram). Participants identified as symptom-free scored 0 on all questionnaires (Table 1). For all questionnaires, higher scores indicated greater symptom severity of disease.

Table 1
Population characteristics and severity questionnaire scores (Katz hand diagram, BCTQ symptom severity, BCTQ functional status) for participants experiencing CTS symptoms and no symptoms with means (ranges). BCTQ indicates the Boston Carpal Tunnel Questionnaire.

	No symptoms ($N = 11$)	Symptoms ($N = 11$)
Age (yr)	26 (23–32)	42 (19–55)
Gender	2 males, 9 females	2 males, 9 females
Katz diagram (0–3 points)	0	1 (0–3)
BCTQ symptom severity (0–4 points)	0	1.9 (1–3.6)
BCTQ functional status (0–4 points)	0	1.3 (0–2.9)

2.2. Motion protocol

Participants performed repeated flexion–extension cycles of the middle finger (Fig. 1) (Tat et al., 2013). Participants were seated with the forearm immobilized in supination to position the ultrasound probe on the palmar surface of the wrist. The hand was supported by padding to maintain the wrist in a neutral posture while grasping a polyvinyl chloride tube (3.5 cm diameter). To isolate motion of the middle finger, the tube was sectioned in the middle to fix all other fingers in a mid-flexed posture. The tube and padding provided physical end ranges to the finger motion and represented full finger flexion. Participants performed the finger motion continuously at a rate of 1 Hz for 10 s (10 flexion and 10 extension movements) in 3 trials. The frequency of finger movement fit the definition for highly repetitive work (Silverstein et al., 1987). A metronome indicated the start of each cycle and the transition between flexion and extension movements. Maximum flexion was defined as the pulp of the distal phalanx contacting the tube, while maximum extension was defined as the fingernail touching the table surface. Maximum flexion occurred at approximately 90° of flexion at both the MCP and PIP joints, representing a tendon excursion of 20–30 mm based on a geometric model (An et al., 1983).

2.3. Ultrasound assessment

A Vivid q BT10 (GE Healthcare, Milwaukee, WI, USA) console and a linear array transducer (12LRS) operating at a central frequency of 12 MHz were used to image the carpal tunnel in each participant. The SSCT associated with the middle flexor digitorum superficialis tendon was assessed. The transducer was positioned at the proximal wrist crease such that it was longitudinal and in line with the tendon. Participants were asked to perform active finger flexion and extensions to identify the tendon.

High resolution grayscale images were collected while the finger was in extension and uploaded to ImageJ software (National Institutes of Health, Bethesda, MD) to perform thickness measurements. Tendon thickness was measured perpendicular to the tendon fibre direction, and SSCT thickness was measured similarly adjacent to the tendon (Fig. 2). We inferred SSCT fibrosis as altered tendon-SSCT gliding function, as fibrosis can only be determined through biopsy and histological examination. We used differential motion between the tendon-SSCT to represent the state of the SSCT interconnections (Ettema et al., 2008). Greater differential motion represented increased damage to the SSCT interconnections and greater fibrosis (Ettema et al., 2008). A dynamic assessment with colour Doppler ultrasound was used to measure differential motion between the tendon and SSCT. The colour Doppler technique has previously been validated for tendon excursion measurements in the carpal tunnel (Oh et al., 2007; Tat et al., 2014a). We used sonographic settings similar to Tat et al.