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Is there a relationship between impaired median nerve excursion and carpal tunnel syndrome? A systematic review

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ABSTRACT

Study Design: Systematic review.
Introduction: It is accepted that the etiology of carpal tunnel syndrome (CTS) is multifactorial. One of the most commonly accepted etiologic factors for CTS is compromise of the kinematic behavior and excursion of the median nerve.
Purpose of the Study: The objective of this systematic review was to establish if there is a relationship between impaired median nerve excursion and CTS.
Methods: A systematic review, following the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines, was conducted. Studies were sought where in vivo median nerve excursion was compared between people with CTS to an appropriate control group. Quality appraisal for each study was conducted using the Newcastle-Ottawa Scale by 2 independent evaluators.
Results: Ten case-control studies using ultrasound imaging to quantify median nerve excursion were included. All studies were rated as of "moderate" methodologic quality having scored 6 or 7 (of 9 stars) for the Newcastle-Ottawa Scale. Seven of the 10 studies concluded that median nerve excursion was reduced in a CTS population when compared with controls.
Conclusion: The literature suggests that median nerve excursion is reduced in people with CTS when compared with healthy controls.
Level of Evidence: 3a.

Introduction

Carpal tunnel syndrome (CTS) is the most commonly reported peripheral neuropathy,[1-4] with a prevalence of approximately 3%-4% in the general population.[2,5] Although the precise etiology of CTS remains unclear,[3,4] it is most likely multifactorial with many different theories postulated as to the exact mechanisms which contribute to common symptoms of numbness, pain, and tingling throughout the distribution of the median nerve.[2,5-7]

In response to postures and movements of daily living, the median nerve (along with the entire peripheral nervous system) is constantly exposed to significant stresses which it must cope with and adapt to.[4] Such stresses can be applied in a myriad of ways that include compressive, tensile, shear stress, or a combination of these.[8] Peripheral nerve excursion, whether in transverse and/or longitudinal planes, is directly influenced by the adjacent joints that impose movement upon it.[9] Nerve movement in this regard is essential to dissipate such mechanical stresses.[8,10]

One of the most commonly accepted etiologic factors for CTS is the kinematic behavior and excursion of the median nerve which is compromised due to a number of different factors. One of these factors being a narrower carpal tunnel volume and an increase in pressure within the enclosed space.[6] This increase in intratunnel pressure is thought to cause compression of the median nerve causing subsequent venous congestion and edema together with an invasion of fibroblasts to the affected tissues which may then lead to the formation of restrictive scar tissue.[5,6] Significant compression of the median nerve may alter the normal sliding and gliding kinematics, as discussed previously.[11] The section of nerve proximal

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to the compression can also become enlarged secondary to increased endoneurial connective tissue, edema, or an obstruction of axoplasmic flow.[5] A number of studies have shown that the cross-sectional area (CSA) of the median nerve is increased in people with CTS compared with healthy controls, this is likely secondary to the factors previously discussed, which would contribute to increased pressure and compression of the median nerve.[12,13] It is also thought that swelling of the flexor tendons and thickening of the subsynovial connective tissue (SSCT) may contribute to an increase in pressure within the carpal tunnel.[1,4]

In conjunction with thickening of the SSCT and the consequential increase in pressure, it is also apparent that the median nerve may become adhered to the SSCT[1,3,14] and or to the transverse ligament.[1,15] Adherence of the median nerve to surrounding tissues and structures may be a further reason for altered excursion of the median nerve in those suffering from CTS. If the median nerve is not free to slide, then segments of the nerve are forced to accommodate the required change in length which may create an increase in local strain.[11] As in CTS, it has been previously shown that an increase in nerve strain of as little as 6% can lead to altered nerve function.[11]

The diagnosis of CTS is primarily made using clinical findings such as Phalen's test, Tinel's sign, and sensory changes in the distribution of the median nerve.[16] Positive clinical findings are commonly confirmed through the use of nerve conduction studies (NCS).[16] The role of medical imaging (ie, ultrasound imaging [USI], magnetic resonance imaging, and so forth) for the diagnosis of CTS is gaining momentum. There is compelling evidence which indicates that the CSA of the median nerve (used as an indirect measure of intraneural edema) at the carpal tunnel inlet is significantly greater in people with CTS and is the most sensitive and specific USI finding for the diagnosis of CTS.[17] Research evidence also concludes that the use of USI as a diagnostic tool for CTS is approaching similar values of diagnostic accuracy to that of NCS[17] with sensitivity of 0.89 and specificity of 0.88 when comparing patients who have CTS confirmed through clinical examination and NCS as a reference standard.[18]

USI has been shown to be a reliable and accurate tool for establishing the excursion of the median nerve.[2] Although the evidence is in agreement about the effectiveness of USI to confirm CTS, there is variability in the reported normative values proposed for median nerve CSA and excursion. This variability may be due to differences in USI techniques reported and/or differences in disease severity and/or duration of those cohorts investigated.[5,17]

In vivo measurement of median nerve excursion can also be measured intraoperatively through insertion of a marker into the median nerve and fluoroscopic imaging during wrist movement.[19] This intraoperative method of imaging is a useful in vivo excursion measurement, although it has been noted that the measurement can only be assumed accurate at the time of surgery and that changes in excursion in relation to healing and scar tissue formation after the surgery are not accounted for.[19]

Purpose of the study

Currently, controversy surrounds whether reduced median nerve excursion is a relevant feature in CTS with some studies suggesting a reduction of median nerve excursion is evident while others suggest otherwise. In light of this controversy,[11] a systematic review of literature is required to examine those studies that have assessed the relevance of median nerve excursion in people with CTS. There is a need to develop a greater understanding about the altered dynamics of the median nerve in CTS and if reduced excursion of the median nerve has a direct relationship with a diagnosis of CTS. The objective of this systematic review was to explore the current literature and establish if a relationship exists between impaired median nerve excursion and CTS.

Methods

Although the protocol for this systematic review has not been registered, this manuscript has been written and formatted in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement.[20]

Information sources and search

An extensive literature search was carried out across a number of different databases to identify literature relevant to median nerve excursion in people with CTS. The databases searched electronically were EBSCO Health, Scopus, MEDline, CINAHL, ProQuest Nursing, Scopus, and Allied Health Source. The keywords that formed the basis of the search (Table 1) were "median nerve excursion," "median nerve movement," "median nerve sliding," "median nerve gliding," "carpal tunnel syndrome," "median nerve entrapment and carpal tunnel." These keywords were expanded through the use of truncation, synonym searching, and proximity searches. Studies found using this search strategy were reviewed using their title and abstracts and the studies meeting inclusion criteria were selected. The search was completed by March 1, 2016, and there was no restriction placed on publication date.

Eligibility criteria

Studies were selected if they met the following inclusion criteria:

- CTS was the primary condition of interest. Each study must have included participants with a diagnosis of CTS which was made either by (1) applying a rigorous diagnostic criteria for CTS (ie, Quality Standards Subcommittee of the American Academy of Neurology and so forth) or (2) following documented clinical assessment (eg, electrodiagnostic testing [ie, NCS], medical imaging, and so forth);
- Use of an assessment tool (ie, medical imaging, surgical visualization, and so forth) which allowed direct, real-time, in vivo measurement of median nerve excursion;
- Comparative study designs (ie, case-control studies, cohort studies, and so forth) comparing a cohort of people with CTS to an appropriate cohort of healthy controls;

Table 1
Study characteristics

Study	Study design	CTS group (n)	Control group (n)	In vivo tool
Erel et al[11]	Case-control	17	19	USI
Filius et al[14]	Case-control	25	14	USI
Hough et al[2]	Case-control	19	37	USI
Kuo et al[6]	Case-control	25	19	USI
Kuo et al[7]	Case-control	40	32	USI
Liong et al[12]	Case-control	12	15	USI
Nakamichi and Tachibana[15]	Case-control	30	30	USI
van Doesburg et al[28]	Case-control	29	29	USI
Wang et al[4]	Case-control	20	20	USI
Yoshii et al[16]	Case-control	51	62	USI

n = participant numbers; USI = ultrasound imaging.

Studies were excluded where the participants did not have a defined diagnosis of CTS (ie, "nonspecific arm pain") and also those articles not published in English.

Study selection

From the initial database search, studies were screened using their titles and abstracts. A review of the bibliography and a prospective "cited by" search, through the Scopus database, was carried out for studies deemed relevant following the database search and any further studies identified using these methods. The full text of these included articles was then examined against the eligibility criteria. This concluded the literature search and selection process.

Data extraction and assessment of methodologic quality

The Newcastle-Ottawa Quality Assessment Scale (NOS) was used to extract data from the included studies and then to critique and analyze the methodologic quality of each study. The NOS is a tool created to assess the risk of bias and methodologic quality of case-control and cohort studies.[22,23] There is controversy regarding the reliability and validity of the NOS.[22] However, a recent systematic review[24] recommended the use of the NOS when assessing the risk of bias and methodologic quality of observational studies such as those of case-control or cohort design; this is also in line with recommendations from the Cochrane Collaboration.[25] Further critique of the reliability of the NOS suggested that it performs better for case-control studies than for cohort studies.[26]

The NOS contains 8 items which are grouped into 3 different categories: *selection, comparability*, and *exposure*. It is scored using a star system, with a maximum of 9 stars able to be awarded over the 3 categories.[22] Studies scored well in the *selection* criteria if both cases and controls were defined and selected well without potential for any bias. In the *comparability* section, studies scored well if confounding factors were controlled for. In this systematic review, confounding factors of interest were age, gender, and position of the hand/wrist during nerve motion assessment (all factors which may influence median nerve excursion and nerve visualization whilst using USI). Studies scored well in the *exposure* section if both participants and controls were recruited using the same methods and the studies had a good response rate.

The method for appraising the quality of the articles was as follows: 2 independent researchers (N.A. and R.B.) critiqued each of the included articles, using the NOS and then compared the scores given for each study. If the scores were different, these were discussed and resolved through consensus. Where consensus was not achieved, a third moderator (R.E.) was available to independently appraise these articles, for final quality control, and consensus was achieved.

Synthesis of results

Following the methodologic review of each included study, a synthesis of the findings of the relationship between median nerve excursion and CTS was conducted. Further synthesis of the main findings with regard to each of the NOS criteria (*selection, comparability*, and *exposure*) was also conducted. Analysis of the overall methodologic quality of the included articles was evaluated using previously reported methods which have categorized studies scoring 8-9 stars, for the NOS, as being of "high," 6-7 stars, "moderate"; and 0-5 stars, "low" quality.[21] Finally, the level of evidence was determined from those detailed in Burns et al.[27]

Results

Study selection

The study selection process is summarized in Figure 1. From the initial database search, reference list cross-referencing and prospective Scopus search 238 studies were screened using their titles and abstracts. Of these studies, 27 were deemed relevant. Following a review of these 27 abstracts, 14 full-text articles were examined against the inclusion and exclusion criteria. Secondary to this process, 4 of the articles were excluded because there was either no direct in vivo measurement of excursion or in one study there was no appropriate control group. The 10 articles meeting the inclusion and exclusion criteria were assessed for methodologic quality and included in this systematic review.

Study characteristics

The characteristics of the 10 studies are shown in Table 2. All 10 studies were of case-control study design, looking at CTS as the condition of interest and used an in vivo tool as a direct measurement of nerve excursion. All the 10 articles used USI as the in vivo tool for the measurement of nerve excursion. Within this body of literature, this finding highlights that USI is the preferred method of measuring nerve excursion.

Methodologic quality

Critique of the methodologic quality of all 10 studies was conducted using the NOS; from which the scoring is shown in Table 3. The 10 studies all scored either 6 or 7 stars for the NOS consistent with "moderate" methodologic quality.[21] In regard to the 3 separate categories within the scoring tool some trends were identified in the 10 studies, all of which are discussed in the following sections (see Selection, Comparability, and Exposure).

Selection

Seven of the 10 studies[2,6,7,11,12,16,28] scored a maximum of 4 stars for the *selection* category indicating that the cases and controls were well described and were selected using suitable inclusion and exclusion criteria, without any potential for bias which is of particular importance for case-control studies. Three studies[4,14,15] were unsuccessful in gaining a maximum rating as they either did not state the recruitment criteria or provided inadequate history of the control subjects.

Comparability

Nakamichi and Tachibana[15] and Wang et al[4] scored 2 stars for the *comparability* category as they controlled for a range of important confounding factors such as age, position of the limb, movement during excursion, position of the transducer and having a blinding procedure in place. Eight of the 10 studies[2,6,7,11,12,14,16,28] scored 1 star, out of 2 stars possible, for the *comparability* category as very few or no confounding factors were controlled for and did not make any mention of blinding procedures. Being that no studies scored zero stars for this section, it can be concluded that attempts were made by all the researchers to control for at least some of the apparent confounding factors to improve the methodologic quality.

Exposure

For the *exposure* category, scores ranged from 1 star up to 3 stars. The studies scoring 3 stars[4,14,15] had rigorous methods of recruiting patients, a matched method for recruiting the control group and

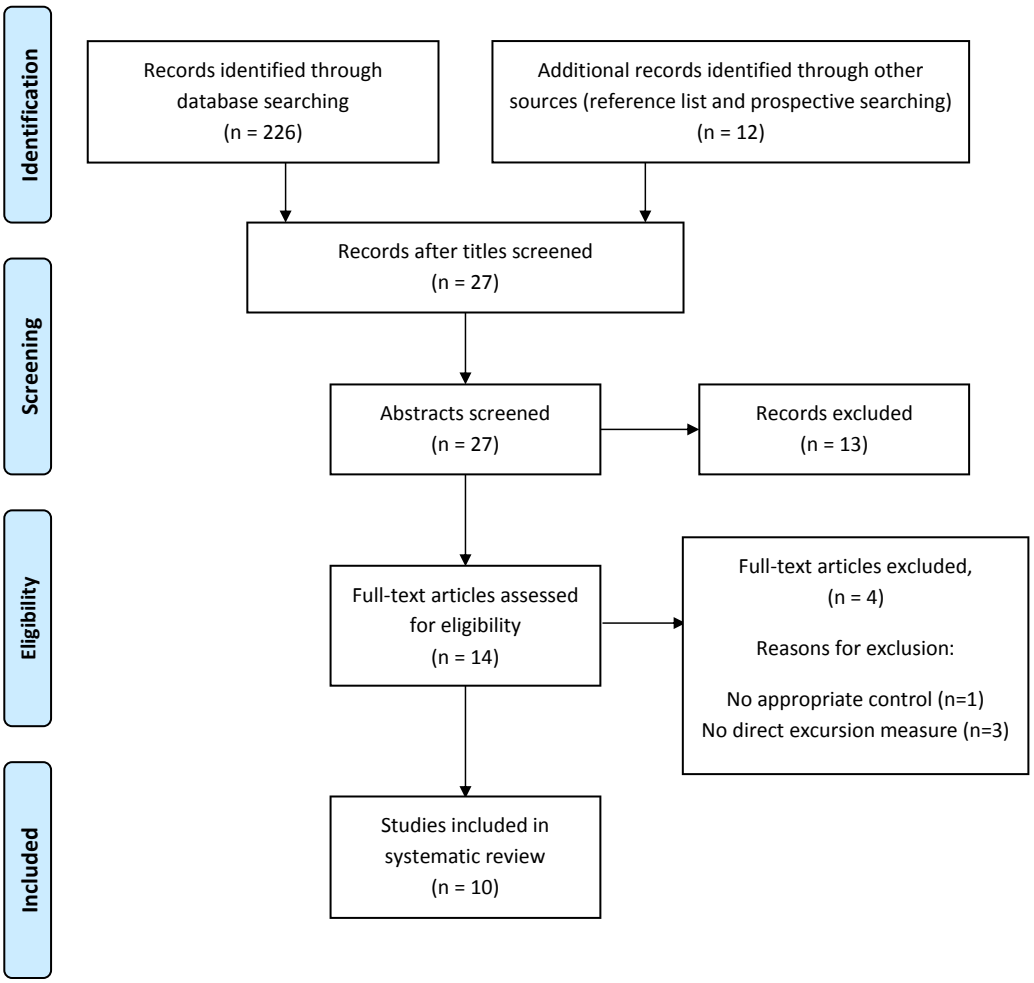

Fig. 1. Study selection flow chart.

finally all had a 100% retention rate. In contrast, the weaker studies in the *exposure* category, scoring 1 or 2 stars, either had different processes for recruiting patients and controls and/or had poor retention rates.

Synthesis of results

The results of the 10 studies are summarized in Table 3. Across the 10 studies, there are varying results in relation to median nerve excursion. Most studies suggested that there is a decrease in excursion of the median nerve, in both transverse and longitudinal directions, in patients with CTS, when compared with an appropriate control group. Hough et al[2] and Filius et al[14] concluded that there was a significant decrease ($P < .001$ for both studies) in longitudinal median nerve excursion in CTS participants compared with control participants. Four studies[4,6,7,15] concluded significant reductions ($P < .05$) in the transverse sliding of the median nerve in CTS participants when compared with control participants.

In contrast, Erel et al[11] found no significant differences ($P > .05$) in median nerve excursion between the CTS participants and control participants. However, these authors demonstrated a significant loss ($P < .05$) in median nerve excursion between the affected and unaffected hands of the CTS group. Finally, van Doesburg et al[28] suggested that there was no significant difference in median nerve excursion between CTS participants compared with controls for movement induced by simultaneous movement of all 4 fingers. However, median nerve excursion was significantly greater ($P < .05$), during individual finger and thumb movements, for the CTS participants compared with the control participants.

Table 2
NOS scores

Study	Selection, (4 stars)	Comparability, (2 stars)	Exposure, (3 stars)	Total score, (9 stars)
Erel et al[11]	4 stars	1 star	2 stars	7 stars
Filius et al[14]	2 stars	1 star	3 stars	6 stars
Hough et al[2]	4 stars	1 star	1 star	6 stars
Kuo et al[6]	4 stars	1 star	2 stars	7 stars
Kuo et al[7]	4 stars	1 star	2 stars	7 stars
Liong et al[12]	4 stars	1 star	2 stars	7 stars
Nakamichi and Tachibana[15]	2 stars	2 stars	3 stars	7 stars
van Doesburg et al[28]	4 stars	1 star	2 stars	7 stars
Wang et al[4]	2 stars	2 stars	3 stars	7 stars
Yoshii et al[16]	4 stars	1 star	2 stars	7 stars

NOS = Newcastle-Ottawa Quality Assessment Scale.

Level of evidence

A systematic review which consists primarily of case-control studies, as this study has, which reports prognostic research (such as this review) is said to be of level 3a evidence.[27] Level 3a evidence promotes either grade B or grade C recommendations. These grades suggest clinicians should take note of the evidence

Table 3
Synthesis of results

Study	CTS group demographics	CTS diagnostic criteria	Control group	Outcome	Results	NOS score
Erel et al[11]	17 idiopathic CTS patients. Age range 30-58 years with a mean age of 45 years.	CTS diagnosis was confirmed clinically and by electrophysiological investigation. In all but one patient, nerve conduction studies were positive; however, this patient met the clinical criteria of CTS. Clinical evaluation included sensory changes in the median nerve distribution of the hand, Phalen's test, Tinel's sign, muscle power, and examination for thenar atrophy. CTS participants were chosen between the ages of 20-60 years and without contributing diseases such as diabetes mellitus or rheumatoid arthritis.	19 control subjects chosen so that the age range and male-female ratio approximately matched the patients. None had a history of upper limb pain and all were examined to exclude upper limb pathology.	Nerve excursion was not significantly different between the control and CTS groups. In CTS patients, there was a significant reduction in transverse sliding when comparing most and least affected sides (40%). This reduction was not significant compared with controls (43%) due to the large variation between subjects.	There was no significant difference between longitudinal nerve excursion in CTS patients (2.2 mm) and healthy controls (2.62 mm; $P > .1$). Significant positive relationship observed between subject height and longitudinal nerve movement. Mean transverse MN translation was 1.55 mm in controls and 0.89 mm in patients. This was not statistically significant ($P > .08$) despite representing a 43% reduction in transverse MN movement. There was a significant reduction in transverse MN movement in CTS patients when comparing their most affected to least affected hand ($P < .05$).	7 stars
Filius et al[14]	18 CTS patients. Seven with bilateral CTS and therefore 25 CTS wrists were examined. Mean age 50 years. Mean BMI 32 kg/m^2.	CTS was confirmed based on clinical examination and NCS. Patients were excluded from the study if they had a history of upper extremity surgery, fractures to the wrist or hand or disorders to the musculoskeletal system.	14 healthy controls. Mean age 42 years. Mean BMI 30 kg/m^2.	In the healthy control group, there was significantly greater MN displacement compared with the CTS group, with a trend of increased MN displacement at a higher tendon excursion velocity. This trend was also seen in the CTS group, however, less obvious.	CTS patients had less absolute ($P < .002$) and relative motion ($P < .001$) of the MN regardless of tendon excursion velocity. In the CTS group, a difference was seen in the displacement of MN between high- and low-velocity tendon excursion ($P = .012$).	6 stars
Hough et al[2]	19 patients with CTS. 8 men and 11 women with an mean age of 57.4.	Recruited patients with a clinical diagnosis of CTS of at least 1 month in duration from local orthopedic clinicians and general practitioners. Patients were excluded if they had required treatment to the neck or upper limb for any injury in the past 6 months apart from CTS, history of major trauma to the neck or limb, systemic neuropathy or were pregnant.	37 healthy controls. 8 men and 29 women with an average age of 48 years.	First direct evidence that reduced longitudinal MN excursion may be present in a substantial number of patients suffering from CTS. It is possible that reduced excursion of the MN contributes to the pathophysiology of CTS.	The patient group showed significantly reduced longitudinal MN excursion with the elbow extended ($P = .013$). The patient group also showed reduced excursion in the nerve/tendon ratios with elbow flexed ($P = .019$) and elbow extended ($P < .001$). CTS patients also showed a mean reduction ($P = .89$) in MN excursion with the elbow flexed.	6 stars
Kuo et al[6]	25 wrists with CTS, age range 22-79 and a mean BMI of 24 $\pm$ 2.77 kg/m^2.	Diagnosis of CTS was confirmed with NCS. Patients were excluded if they had cervical radiculopathy, diabetes mellitus, hypothyroidism, or arthritis.	19 wrists with no clinical signs or symptoms of CTS. Age range 32-51 years and an average BMI of 23.6 $\pm$ 2.47 kg/m.^{2}	The MN moved toward the ulnar side in finger flexion and toward the radial side on finger extension. Implications that decreased MN mobility is correlated with blocked median nerve conduction velocity.	Transverse sliding of the MN during finger flexion or extension was reduced in CTS patients compared with controls ($P < .05$). Compared with the normal MN, the MN in CTS patients was subject to internal compression due to increased pressure within the carpal tunnel which resulted in reduced mobility with finger motion.	7 stars

(*continued on next page*)

Table 3 (*continued*)

Study	CTS group demographics	CTS diagnostic criteria	Control group	Outcome	Results	NOS score
Kuo et al[7]	40 wrists with CTS.	Diagnosis of CTS was confirmed with NCS. Patients were excluded if they had cervical radiculopathy, diabetes mellitus, hypothyroidism, or arthritis.	32 wrists with no clinical signs or symptoms of CTS.	The MN moved toward the ulnar side in finger flexion and toward the radial side on finger extension. The temporal changes in transverse sliding of the median nerve within the carpal tunnel were found to be correlated with the presence of CTS and its severity.	Transverse sliding of the MN during finger flexion or extension was reduced in CTS patients compared with controls ($P < .001$). The representative transverse sliding patterns of the median nerve during finger movements were demonstrated to be useful for quantitatively estimating median nerve dysfunction in CTS patients.	7 stars
Liong et al[12]	12 clinically diagnosed patients with mild CTS. 8 females and 4 males. Age range 30-45 years.	Recruited patients with mild CTS symptoms as assessed by the Boston Carpal Tunnel Questionnaire. Patients were excluded if there was a history of neurologic conditions, hand trauma, or diabetes.	15 asymptomatic volunteers. 11 males, 4 females. Age range 30-45 years.	Insight into the nerve tendon dynamics associated with CTS and into the changes that occur when mild CTS develops. In particular, it was established there is a predominant general motion that exists for individual finger flexion and that there is significantly reduced MN displacement in subjects with CTS.	CTS participants showed less nerve displacement with 0.852 mm (0.369), 0.971 mm (0.459), and 1.36 mm (0.913) in thumb, index finger, and middle finger flexion, respectively. This is in comparison to the displacement shown in normal subjects of 1.21 mm (0.461), 1.27 mm (0.637), and 1.52 mm (0.646), respectively. MN displacement increased from thumb flexion, index finger flexion and middle finger flexion in ascending order, with the significant difference between thumb and middle finger flexion ($P = .0280$).	7 stars
Nakamichi and Tachibana[15]	30 wrists of 15 women with idiopathic bilateral CTS. Mean age 53.9 years.	Subjects were diagnosed with bilateral CTS via sensory testing, Phalen's test, muscle testing, and electrophysiological testing. The CTS etiology was determined as idiopathic by excluding rheumatoid arthritis, chronic renal failure under hemodialysis, endocrine, or metabolic disorders including diabetes, gout, amyloidosis or hypothyroidism, Colles fracture, ganglion, calcific deposition, and osteoarthritis.	30 control wrists from 15 age-matched healthy women. Mean age 54.4 years.	The method used is insufficient to evaluate the mobility in some healthy individuals. CTS does not necessarily develop due to decreased mobility alone. In some patients CTS may be as a result of other factors, even if mobility is fair.	The MN showed less sliding ($P = .0001$) in CTS patients (0.37 ± 0.34 mm) than in controls (1.75 ± 0.49 mm) between flexion and extension.	7 stars
van Doesburg et al[28]	29 volunteers with idiopathic CTS. 18 women and 11 men. Age range 26-70 years with a mean age of 51.1 years. All but 2 volunteers had bilateral CTS.	CTS was clinically diagnosed and was confirmed by electromyography. CTS patients were excluded if their medical records showed a history of systemic disease associated with a higher incidence of CTS or any trauma or surgery of the lower arm.	29 healthy volunteers with no history of CTS. 15 women, 14 men. Age range 22-67 years with a mean age of 35.5 years.	There is a changed motion pattern of the MN and flexor digitorum superficialis tendons in the carpal tunnel in CTS patients compared to normal subjects. Results show greater motion of the MN in CTS patients' than in normal subjects while other studies show irregular and small transverse displacement.	In fore finger motion there was no difference in MN motion direction between normal subjects and patients. In middle finger motion, the MN moved more ulnarly in CTS patients than controls ($P < .0001$). In index finger motion, the MN and the FDS II tendon moved more ulnarly in CTS patients compared to controls ($P = .038$). In thumb motion, the MN moved dorsoradial in patients, whereas it moved palmarly and ulnarly in controls ($P < .05$).	7 stars

Wang et al[4]	13 patients with clinically diagnosed CTS. Six men, 7 women, age range 41-60 years with a mean age of 50.9 years.	Clinical diagnosis according to the diagnostic criteria of the Quality Standards Subcommittee of the American Academy of Neurology. 7 patients had bilateral CTS and so 20 wrists with CTS were included in the study. Patients were excluded if they had arthritis, degenerative joint disease in the hand or wrist, flexor tendonitis in the hand or wrist, space occupying lesions of the wrist, coexistent neurologic diseases, diabetes mellitus, history of trauma to the hand or wrist, and other systemic diseases.	10 healthy volunteers. 4 men, 6 women, age range 25-56 years with a mean age of 39.1 years. Both wrists were evaluated in controls and thus 20 control wrists were examined.	With maximal wrist flexion with or without finger flexion and maximal ulnar deviation the MN deformed and moved less in CTS patients than healthy controls. Mobility of the MN was decreased in patients with CTS which may be due to adhesion of the median nerve to the fibrosed SSCT.	A significant difference in the mean MN displacement was found between CTS patients and controls for wrist flexion with fingers extended ($P < .01$), wrist extension with fingers extended ($P < .05$), and ulnar deviation with fingers extended ($P < .01$). There was no significant difference between groups for movements of finger flexion ($P = .217$) or wrist extension with fingers flexed ($P = .106$).	7 stars
Yoshii et al[16]	51 wrists of 28 idiopathic CTS patients. 22 women, 6 men, age range 43-85 years, mean age of 60.9 years.	Diagnosed by both clinical findings and NCS. Excluded if they reported a history of cervical radiculopathy, arthritis, flexor tendonitis, gout, hemodialysis, obesity, sarcoidoma, amyloidosis, or trauma to the arm.	62 wrists of 31 asymptomatic volunteers. 26 women, five men, age range 22-64 years with a mean age of 42.8 years.	There is a changed pattern of MN motion in association with middle finger, index and thumb motion when comparing controls and patients.	During finger flexion, the MN for control participants moved 2.3 mm in the ulnar direction compared with the CTS participants moved 1.98 mm ($P = .06$). MN displacement toward the palmar side was significantly smaller ($P < .01$) in the CTS group.	7 stars

BMI = body mass index; CTS = carpal tunnel syndrome; FDS = flexor digitorum superficialis; kg = kilograms; m = mass; mm = millimeters; MN = median nerve; NCS = nerve conduction studies; NOS = Newcastle-Ottawa Quality Assessment Scale; SSCT = subsynovial connective tissue.

while being aware of other research.[27] Therefore, following this review, it would be appropriate for clinicians to consider that impaired median nerve movement may be an influencing factor in the etiology of CTS.

Discussion

Summary of evidence

The results of this review show that most studies which have assessed median nerve excursion in people with CTS support the theory that reduced nerve excursion is a relevant feature of this condition. Five[2,4,12,14,15] of the 6 studies which examined longitudinal median nerve excursion concluded significant reductions in people with CTS compared with controls. Of the 4 studies which examined transverse median nerve excursion (ie, ulnar-radial, superior-inferior), 3[6,7,16] concluded significant reductions in people with CTS compared with controls.

However, it is apparent that controversy remains as to the true influence of reduced median nerve excursion for people with CTS. For example, van Doesburg et al[28] suggested the transverse excursion of the median nerve, when induced by different combinations of finger movements, is greater in people with CTS than in the control groups. This particular study highlighted the different patterns of excursion (including amount and direction) for the median nerve in people with CTS as compared with control participants. It was suggested that the relationship between the median nerve and surrounding structures (ie, flexor tendons of the fingers) is altered in people with CTS which may explain the different excursion patterns.[28]

Furthermore, Erel et al[11] found insignificant differences in the transverse and longitudinal excursion of the median nerve when comparing a CTS population with a healthy control group. Erel et al[11] did, however, find there was a significant reduction in median nerve excursion in people with bilateral CTS when comparing their most affected hand to the least affected hand.

Of note, the studies by Erel et al[11] and van Doesburg et al[28] scored 7 (of 9) stars on the NOS indicating “moderate” methodologic quality.[21] Patient demographics in these studies were fairly well matched to the control group and do not differ greatly from the demographics in the other 7 studies. However, van Doesburg et al[28] do assert that insufficient power may have been a contributing factor. A further weakness discussed in the study was that the mean age of the control and participant groups differed by 15 years and has the potential to introduce bias and detect age-related changes associated with CTS excursion as opposed to CTS-related excursion changes.[28] In comparison, Erel et al[11] did not have any demographic differences of interest. However, Erel et al[11] did report a 43% reduction in transverse excursion between the CTS group and controls which possibly did not reach statistical significance because of the large variation between subjects.

As some studies did not achieve 4 stars in the *selection* category, of the NOS, there is the potential for selection bias as there is an increased chance of demographic differences between the case and control groups. Demographic differences such as age and gender are important to consider as these may impact on nerve excursion. Furthermore, the study by Nakamichi and Tachibana[15] used women only (both the cases and controls) and therefore limiting the generalizability of their findings.

Those studies scoring 3 stars in the NOS *exposure* category[4,14,15] can be far more confident in assuming that participants from both cohorts (CTS and healthy participants) have been recruited using the same protocols and care was taken to ensure the CTS participants had a definitive diagnosis of CTS. The weaker studies in the *exposure* category (scoring 1 or 2 stars[2,6,7,11,12,16,28]) either had

different processes for recruiting patients and controls and/or had poor retention rates. In most of the studies, control participants were selected with an attempt to match important characteristics such as age and gender to the participants in the CTS group. Furthermore, confirmation was made that control participants had not been diagnosed with CTS nor had any comorbidities or trauma to the arm. Controlling for these confounding factors is crucial to accurately state that results do or do not show a difference between the participants with CTS and the control participants.

One of the most important aspects of this review was to look at the methods of in vivo measurement that the studies used. In all the studies, nerve excursion was measured using USI. However, there was a significant variability in the methods used across the studies. The ultrasound equipment used along with the analysis of USI differed between studies.

Although all studies used standardized testing positions (in regard to participant position, limb position, scanning location, and so on), there were differences. For example, the position of the elbow varied with some studies using full extension,[11,15] some being in various degrees of flexion[12,14,16] and others not mentioning position of the elbow.[6,28] Several studies standardized the shoulder position,[2,4,11] whereas others did not mention this specifically.[6,12,14,16,28] As the median nerve travels down the entire upper limb, the position of the limb joints (ie, elbow and shoulder) would have had a direct influence on the amount of median nerve excursion. Furthermore, the wrist, finger, and hand movements that were used to induce median nerve excursion differed between the studies. Some studies used movements of the metacarpophalangeal joints[11] or interphalangeal joints[15] while other studies used a combination of metacarpophalangeal and interphalangeal joint movement.[2,6,12,14,16,28] One study looked at wrist and finger movement.[4] This heterogeneity in methods makes direct comparison of the results of these studies problematic.

As all 10 studies scored either 6 or 7 stars on the NOS, it can be concluded that the strength of methodologic quality of these studies was “moderate”.[21] Furthermore, as all the reviewed studies were of case-control design, the level of evidence that can be reported following this review is level 3a evidence.[27] With regard to the clinical implication of this systematic review, level 3a evidence promotes either grade B or C clinical recommendations meaning clinicians should take notice of the evidence and be cognizant of the results and should also be aware of other research in this area.[27] From this review, it would be appropriate for clinicians to consider that reduced median nerve excursion may play a role in the etiology and pathophysiology of CTS. It may therefore be relevant to include treatment options that would aim to directly influence median nerve excursion, such as neural mobilization exercises and promotion of optimal upper limb movement and function. Further research and creation of an USI-based classification model with defined cutoff values, a standardized measurement protocol and a cost-benefit analysis of the procedure will promote the use of USI as a diagnostic tool for CTS.[29]

Despite efforts made toward rigorous study selection, synthesis, and analysis of results, this review has some limitations. First, the selection criteria were set specifically for comparative studies (ie, case-control and cohort design). This review did not seek to examine randomized controlled trials. It is possible that there are RCTs available that have examined interventions for CTS that have data available which make direct comparisons regarding median nerve excursion between healthy and CTS populations. With the included studies all of case-control design, the level of evidence that can be concluded from this review is limited to 3a evidence with recommendations at grades B or C. As well as this, the variability in methods across all studies meant further analysis via meta-analysis was not possible.

Conclusion

In conclusion, although controversy remains, most current literature suggests that there is a degree of reduced median nerve excursion evident in the population of CTS sufferers when compared with healthy controls. Following this review, it is apparent that further high-level research is needed to accurately establish the role impaired median nerve excursion plays in CTS. Well-designed randomized control trials would be useful to further build this evidence base.

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