

# A systematic review of the methodology of sonographic assessment of upper limb activities-associated carpal tunnel syndrome

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### Abstract

**Background:** Various upper limb activities were speculated to be associated with the development of carpal tunnel syndrome (CTS). Nonetheless, there are currently no standardization on the uses of parameters in CTS assessments, nor are there any conclusive findings regarding the usefulness of various sonographic measurements in studies of different upper limb activities. In this review, we intend to evaluate the methodology of assessing CTS induced by upper limb activities with ultrasonographic technique and provide corresponding suggestions.

**Methods:** Clinical studies on the association between upper limb activities and prevalence of CTS using ultrasonography were recruited in a database research on the basis of a procedural selection criteria and reviewed. The following qualitative items were extracted: characteristics of studies, scanning methods, selection of sonographic parameters, and related article findings.

**Results:** Eleven studies were qualified for this review. Three studies were computer keyboard typing related, five studies were electronic device related, and three studies were wheelchair-related. All sampled articles included cross-sectional area (CSA) at the pisiform level. The swelling ratio (SR) and flattening ratio (FR) at the hamate level are also used in most studies in addition to the CSA at the pisiform level. The effectiveness of such parameters is subjected to various confounding factors such as age, weight, body mass index, and wrist anthropometrics, suggesting CSA and SR with sufficient levels had significant values as sonographic parameters. Values of parameters were found affecting symptomatic signs and hand dominance.

**Conclusion:** Ultrasound scan is a suitable tool to assess the relationship between upper limb activity and CTS. CSA at the pisiform level and SR and the FR at the hamate levels are generally suitable in upper limb–associated CTS investigations. Specific study designs are required to eliminate different confounding factors accordingly.

Keywords: Carpal tunnel syndrome; Hypertrophy; Ultrasonography

# **1. INTRODUCTION**

Carpal tunnel syndrome (CTS) is a wrist pathology with the highest prevalence in the reported nerve compression disorders.<sup>1</sup> The population prevalence of clinically certain CTS was found to be 3.8% in a Swedish study.<sup>2</sup> The impairment by the median nerve is initiated by the mechanical compression by the swelling

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and hypertrophy of connective tissue that increase the intracarpal canal pressure.<sup>3,4</sup> Most patients with CTS experience pain, numbness, and tingling sensations in the hands and arms. Upper limb activities-related CTS is mostly due to general causes instead of local post-traumatic deformation. Armstrong et al. stated that people who perform repetitive extreme excursions at their wrists and with a direct external force are in a group of higher risk in development of CTS.<sup>5,6</sup> CTS plays a leading role in the work-related overload syndromes at the upper limbs in addition to those due to recreational activities.7 Symptoms of CTS are proved to lower patients' ability to carry out workrelated activities, which will probably end in work disability.8 Distribution of pain to the median nerve-supplied regions plays an important role as a clinical feature, yet it is likely to be overlooked by patients.<sup>9,10</sup> Atroshi et al. stated that a median mononeuropathy is demonstrated in approximately 15% of the general population with no report of any symptoms of hand.<sup>2</sup> This brings out the importance of diagnostic tools. Simple clinical tests such as Phalen's and Tinel's tests both have a low sensitivity and specificity and Tinel's sign was considered worthless by some respondents of a study.9 Nerve conduction study is a more

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advanced examination than the clinical tests, providing objective information of median nerve compression.<sup>9</sup> However, the considerable numbers of false-positive and false-negative results and varying normative cutoff for abnormality make nerve conduction study a controversial role.<sup>11</sup> Imaging tests on the structures of the carpal tunnel have emerged as the alternatives giving accurate differential diagnosis in last two decades.<sup>12-14</sup> Magnetic resonance imaging (MRI) has been recognized as a diagnostic modalities for CTS, and the accuracy and reliability of MRI on CTS assessment have been assessed by Middleton et al.<sup>15</sup> However, clinicians seldom use MRI in routine examination for CTS because of the high cost and long duration of scanning.

Ultrasonography is a non-invasive and superior to MRI for its cost-effective and real-time nature; we notice the lack of review and pool of methodological studies evaluating the ultrasonographic assessment in a qualitative manner. This study focused on ultrasonography where the ultrasound equipment and probes have undergone immense improvement in recent years. An article by Impink et al. showed the reliability of ultrasound as a tool to assess median nerve characteristics.<sup>16</sup> Differentiation between CTS and other neuropathies could be achieved by using ultrasound. Quantitative results of sonographic parameters allow an objective analysis for CTS diagnosis. Nonetheless, the way of obtaining measurements has not yet fully standardized and still require attentions together with the new equipment and techniques available, giving differences in study design.<sup>15</sup>

Recent studies reported the application of various sonographic parameters for assessing CTS. As summarized by Hobson-Webb and Padua, frequently assessed observation parameters for the median nerve changes include increase in nerve cross-sectional area (CSA), nerve flattening ratio (FR), wrist-to-forearm ratio, and inlet-to-outlet ratio.<sup>17</sup> Changes in wrist or carpal tunnel condition such as wrist mobility, vascularity around median nerve, and flexor retinaculum bowing are also commonly seen in diagnosis. A few systematic review and meta-analysis were performed on the performance of ultrasonography for the diagnosis of CTS as well.<sup>18,19</sup> These studies focused on the determination of accuracy, sensitivity, and specificity and were analyzing quantitatively.

In a hope to discuss how subject positioning is varied between different sonographic carpal tunnel assessment and the design of data collection. Another main aspect of this study is to analyze the values and confounding variables of each carpal tunnelrelated sonographic parameters for median nerve assessment. To address the mentioned problem, this review study attempts to suggest a guideline for future sonographic carpal tunnel assessment in the methodology and the process of data collection.

## 2. METHODS

#### 2.1. Literature search

This systematic review was guided by the Preferred Reporting Items for Systemic Reviews and Meta-Analyses statement for conducting literature review and presentation of results.<sup>20</sup> A computer-based research was conducted using PubMed as the database of articles published within 2006 and 2020. Only studies in English or with an English version were included. The research strategy included clinical studies on the association between upper limb activities and CTS using ultrasonographic assessment. There were some exclusions from this review: articles on participants diagnosed with CTS, and articles on participants with surgical history at upper limbs, articles on nerve conduction study as the assessment method, articles on systematic review or meta-analysis or case report or case study, and articles on treatment of CTS.

The employed keywords in searching for articles are listed in the following: "ultrasonography," "carpal tunnel syndrome," "median nerve," "sports," "keyboarding," and "electronic device." The above key words assembled a code to be applied to the search engine of database. The search code was followed by several key words with a "NOT" in front to perform the exclusions: "surgery," "systematic review," "meta-analysis," "case report," "case study," "review," "treatment," and "nerve conduction study."

#### 2.2. Study selection and snowball sampling

Selected articles were initially screened by titles and abstracts following the inclusion and exclusion criteria. The same strategy was applied for snowball sampling to enrich the harvested articles. Snowball sampling has been suggested for its usefulness for extending a systematic literature study in particularly.<sup>21</sup> Both backward and forward snowballing were achieved for more reference article recruitment. Backward snowballing makes use of the reference list of each included paper, where articles in the reference list were screened. In forward snowballing, the articles citing the included papers were evaluated.

#### 2.3. Data extraction and analysis

Objectives of the review study were confirmed and agreed among investigators before data extraction. The design and data collection variations of each study, in particular the sonographic CTS parameters, were observed and analyzed. The sampled studies were analyzed both collectively and individually according to the upper limb activity type. No statistical analysis was performed due to the qualitative nature of this review. In light of the focus on the methodology analysis of this review, risk-ofbias assessments were also omitted in this review.

# 3. RESULTS

A total of 473 articles were initially identified by the PubMed keyword searching, where 7 of them were selected after screening, followed by snowball sampling resulting in 5 more articles included into consideration. A total of 11 clinical trials were included in this systematic review after a procedural selection criteria for eligibility (Fig. 1). Table 1 summarized the characteristics of all studies selected. Baseline variables were related to the subject characteristics such as age, weight, body mass index (BMI), and wrist circumference at certain extent which was in line with previous studies. One concluded that age, gender, and hand dominance were factors of the laterality of CTS.<sup>33</sup> There was a highest prevalence of CTS at the old-aged group of people.<sup>34</sup> It was confirmed in another study that BMI and wrist anthropometrics as independent risk factors for CTS. Greater BMI, higher wrist, and shape indices were found significant in patients with CTS than in the control group.<sup>35</sup> Obese subjects with BMI over 29 were found to be 2.5 times more likely than thin subjects with BMI <20 having CTS.34

#### 3.1. Study design

Studies included focused on upper limb activities frequently related to CTS from three domains: keyboarding, using electronic devices, and activities with a wheelchair (Table 1). Design of studies could be classified into two main genres, where 9 out of 11 articles belonged to cross-sectional study with task(s) performed and remaining 2 were cohort study. Besides the negative group of subjects in cohort studies, only one cross-sectional study involved control group of subjects. Multiple scans with more than two time points were adopted by half of the task performing studies. Postrest scan after a certain period of performing the task was conducted in three articles only.

#### 3.2. Scanning methods

Items related to the scanning methods were included in Table 2 with alphabetical orders. Subject positioning was listed from

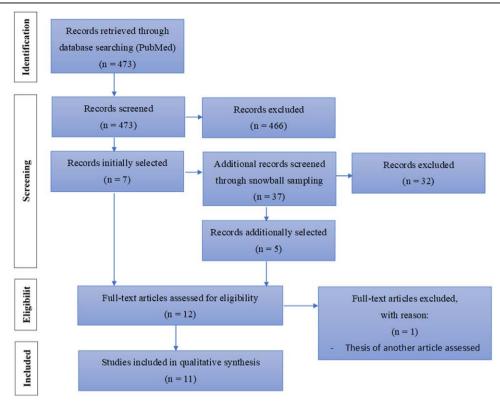


Fig. 1 Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) flow diagram. The reference article searching was conducted following the PRISMA guideline. The search was initiated with PubMed followed by Snowballing using Google Scholar for expansion.

distal to proximal locations. With respect to the instrumentation, almost all studies utilized a high-frequency linear probe (Table 2). The general subject positions adopted were sitting with neutral position of wrist, supinated forearm, and 90° flexion of elbow.

# 3.3. Selection of sonographic parameter measurement

A high variability in terms of parameters was exhibited by the included studies (Table 3). CSA of median nerve appeared in 10 out of 11 studies.<sup>22–27,29–32</sup> SR and FR were used frequently following CSA. SR was calculated by the ratio of CSA at pisiform to CSA at distal radius, whereas FR was obtained by dividing the major axis by the minor axis of the median nerve. In addition, median nerve perimeter, diameters, and circularity were considered by some articles.<sup>26,30,31</sup> Relative parameters of median nerve and structure other than median nerve were also assessed. <sup>26,28,31</sup> Almost all variables were taken at two or more levels, with pisiform as the most common one. Six studies only performed the measurement at one location.<sup>23,25,26,28,30,32</sup>

# 3.4. Bilateral or unilateral wrist scans and hand dominance

Bilateral wrist measurement was taken in five studies (Table 1). For studies using unilateral scans, only nondominant hand was assessed in two studies.<sup>24,29</sup> These were done at an attempt to eliminate other reasons of developing CTS other than performing the activity. FR had no significant difference with the hand dominance.<sup>27</sup> This was consistent with another study showing significant difference in FR between both hands at baseline only but not after task.<sup>25</sup>

# 3.5. Baseline variables with confounding factors

Several confounding factors were concluded to be affecting baseline variables (Table 4). Age, weight, BMI, and wrist circumference were found to be significantly related to values of parameters at baseline.<sup>24,25,27,29</sup> Regarding the characteristics of recruited subjects, six studies invited participants from young age group (18–30 years) and two from middle-aged group (31– 59 years). Remaining three studies involved mixed-age group of participants (18–65 years) (Table 1). Only one study found no significant relationships between baseline median nerve variables and subject characteristics.<sup>22</sup>

# 4. DISCUSSION

# 4.1. Subject positioning

Ultrasound being one of the most user-dependent imaging modalities, slight difference in subject positions and scanning positions could result in a large variation of results. Reviewing the subject positions of various regions of the upper limb, there were some positions that investigators were generally adopting.

Studies proved that there was a significant displacement of the median nerve within carpal tunnel at certain wrist and finger positions on the transverse sonographic scan in healthy subjects.<sup>36,37</sup> The result from a study by Wang et al. stated wrist palmar flexion and ulnar flexion induced significant deformation of median nerve as well.<sup>38</sup> The above deduced that extension and flexion of wrist pose an effect on the variables measured. It was also found that transverse displacement of median nerve was affected by finger motion.<sup>37</sup> However, the findings on finger position from this study did not conclude a general position adopted. The reason for being unable to draw a general conclusion is related to the considerable number of studies not mentioning the position of fingers employed.

Most included studies adopted a supinated forearm position during the ultrasound scan. Use of a forearm supination was supported by a study by Echigo et al.<sup>39</sup> Less nerve gliding

## Table 1

#### Characteristics and design of the included studies

Authors	Activity	Characteristics of	Comparison between symptomatic and asymptomatic		Experimental group(s)/target	Number of measuring time	Performance	•	Unilateral (dominant/ nondominant)/ bilateral measurement
Authors	Activity	subjects	subjects	group	cohort	points	of task(s)	scan	of wrist
Impink et al. <sup>22</sup>	Wheelchair basketball	N = 28 Age: 40.3 $\pm$ 8.86 Include symptomatic subject	Yes	No	N/A	2	Yes	No	Unilateral (nondominant)
Lai et al. <sup>23</sup>	Electronic device	N = 31 Age: 18 - 25 Exclude symptomatic subject	No	No	N/A	2	Yes	No	Unilateral (dominant)
Impink et al. <sup>24</sup>	Wheelchair propulsion	N = 50 Age: 18 - 65	Yes	No	N/A	8	Yes	Yes	Unilateral (nondominant)
Toosi et al. <sup>25</sup>	Keyboarding	Include symptomatic subject N = 20 Age: 22 - 45 Exclude symptomatic subject	No	No	N/A	3	Yes	No	Bilateral
Shim <sup>26</sup>	Smartphone	N = 20 Age: 22.3 $\pm$ 0.8 Exclude symptomatic subject	No	No	N/A	2	Yes	No	Not mentioned
Toosi et al. <sup>27</sup>	Keyboarding	N = 37 Age: 19 - 46 Exclude symptomatic subject	No	No	N/A	4	Yes	Yes	Bilateral
Inal et al. <sup>28</sup>	Smartphone	N = 102 Age: 18 - 23 Exclude symptomatic subject	No	Smartphone nonuser	High and low smartphone users	N/A	No	N/A	Bilateral
Hogaboom et al. <sup>29</sup>	Wheelchair transfer	N = 30 Age: 42.2 $\pm$ 13.2 Exclude symptomatic subject	No	No	N/A	2	Yes	No	Unilateral (nondominant)
Loh et al. <sup>30</sup>	Keyboarding	N = 15 Age: 24.8 ± 2.3 Exclude symptomatic subject	No	Yes	Typing I and II groups	8	Yes	Yes	Bilateral
Woo et al. <sup>31</sup>	Electronic device	N = 48 Age: 18 - 25 Exclude symptomatic subject	No	Nonintensive user	Intensive user	N/A	No	N/A	Bilateral
Rania et al. <sup>32</sup>	Smartphone	$\begin{split} &N=56\\ &Age: 20.36\pm1.6\\ &Exclude symptomatic subject \end{split}$	No	No	N/A	2	Yes	No	Unilateral (dominant)

was observed in forearm supination and entrapment of median nerve tended to occur in forearm pronation. As a result, it is likely for forearm supination to cause less deformation or distortion due to positioning on the median nerve during the scan. Moving proximally from the forearm, median nerve is likely to be unloaded in a posture with the elbow flexed.<sup>40</sup> The nerve is then under little tension in elbow flexion. Indeed, a position with extended and abducted arm and adducted shoulder are used together with flexed elbow in many clinical situations. Our finding on elbow position was in an agreement with the result of the above study that also used a 90° flexion of elbow.

#### 4.2. Ultrasonic measurements and imaging signatures

## 4.2.1. Cross-sectional area

CSA was the most common variables measured yet with the largest variety of scanning locations among reviewed studies. Regarding the included study with largest number of levels scanned, the significant differences in four out of five locations were explainable by previous studies.<sup>28,41</sup> Measurement from several levels may establish intercorrelated relationships to demonstrate the characteristics of CTS on median nerve such as the

physiology of the symptoms appeared. It was suggested by multiple studies that the largest CSA obtained within the whole carpal tunnel region maybe more accurate than focusing at certain level.<sup>42,43</sup>

Enlargement of CSA at the pisiform level found after analysis matched with the pathology involved, which somehow established value of CSA. Pisiform is anatomically at the carpal tunnel inlet. Two previous studies stated that nerve just proximal to the entrapment site are usually having swelling.<sup>44,45</sup> For CTS, nerve entrapment occurs at the carpal tunnel so pisiform matches the location that is proximal to the entrapment site. Additionally, CSA at distal radius was found to have a decrease after activity.<sup>29</sup> The study explained that the decrease had shown the swelling of median nerve that did not extend to the level of distal radius so it matched with the pathology. However, only one study had this opposite direction of change of CSA at these levels. Future studies could have more insights into the direction of change.

# 4.2.2. Swelling ratio

When extracting CSA at all scanning levels is not possible, pisiform and distal radius level should be prioritized. A new

# Table 2

Authors	Method of locating median nerve	Subject position (fingers)	Subject position (hand)	Subject position (wrist)	Subject position (forearm)	Subject position (elbow)	Subject position (other)	Subject position (sitting/ lying)	Transducer and frequency
Impink et al. <sup>22</sup>	Manual tracing	N/A	Neutral posture	N/A	Neutral posture	N/A	N/A	N/A	10–22 (MHz) linear array transducer
Lai et al. <sup>23</sup>	Not mentioned	Fully extended	Supinated	Neutral position (0°), 15°, 30°, 45°	Rested on table	90° Flexion	Shoulder slightly abducted	Sitting	L12-5 (MHz) linear array transducer
Impink et al. <sup>24</sup>	Manual tracing	Relaxed	Supinated	Neutral position	Supinated	90° Flexion	Upper arm relaxed and fully adducted with no internal or external rotation	Sitting	5–12 (MHz) linear array transducer
Toosi et al. <sup>25</sup>	Not mentioned	Relaxed	N/A	Neutral position	Supinated	90° Flexion	Upper arm relaxed and fully adducted with no internal or external rotation	Sitting	5–12 (MHz) 50 mm linear array transducer
Shim <sup>26</sup>	Not mentioned	N/A	Supinated	Neutral position	Rested on table	90° Flexion	Shoulder comfortably maintained	Sitting	7–10 (MHz) high- frequency linear probe
Toosi et al. <sup>27</sup>	Manual tracing	Relaxed	Adducted without internal and external rotation	Neutral position	Supinated	90° Flexion	N/A	Sitting	5–12 (MHz) linear array transducer
Inal et al. <sup>28</sup>	Manual tracing	N/A	Supinated	At rest	Semi-flexed	N/A	N/A	Sitting	7–13 (MHz) linear array probe
Hogaboom et al. <sup>29</sup>	Manual tracing	Relaxed	N/A	Neutral position	Supinated	90° Flexion	N/A	Sitting	Not mentioned
Loh et al. <sup>30</sup>	Manual tracing	N/A	N/A	Neutral position	Supinated	30° Flexion	Arm rested on table	Sitting	5–13 (MHz) 12L- RS transducer
Woo et al. <sup>31</sup>	Manual tracing	Fully extended	Supinated	Neutral position	Rested on table	90° Flexion	N/A	Sitting	L12-5 (MHz) Linear array
Rania et al. <sup>32</sup>	Not mentioned	Thumb moving to text	Neutral posture	Neutral position	Rested on table, supinated at 45°	90° Flexion	Shoulder slightly abducted	Sitting	HRUS (13 MHz MTurbo system)

parameter SR could be generated to demonstrate and compare the swelling of median nerve.<sup>27</sup> The effectiveness of SR to detect changes of median nerve was explained by previously mentioned physiology of pisiform level as the entry point causing the nerve entrapment. It was noted that SR increased significantly in CTS patients in some studies.<sup>46,47</sup> It is of elevated importance of SR on studies looking for the association between activity and presence of CTS. SR could be exaggerated by the performance of activity, which was agreed by the result of the study by Altinok et al.<sup>48</sup>

# 4.2.3. Flattening ratio

Unlike CSA and SR, the role of FR in assessing CTS was controversial. On the one hand, there were no significant differences of FR at most of the levels. It was found in previous study that there was a low reliability at the hamate level as well.<sup>27</sup> Having no changes in FR could be explained by the limitation to expand for the median nerve due to intraneural edema of median nerve caused by repetitive movements of wrist and finger. As the increase in CSA did not occur along the two axes of diameter, which was in line with our finding, the two diameters changed proportionally giving the same FR value.

On the other hand, a significant decrease of FR collected at the hamate in symptomatic subjects were found in a study though a small number of data available. A study by Marquardt et al.<sup>49</sup> found the application of compressive force impacted FR of median nerve significantly. Finding of the included article was consistent with the finding of this study. The decrease in FR was

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an evidence of a rounder shape of median nerve, which could be due to swelling of median nerve correlated to increase in CSA.

# 4.3. Postrest scan

Taking measurement after certain period of performing activity showed a significant result of the postacute effect in the studies. Returning of values of parameters back to the baseline was in the completion of showing the overall changes of median nerve. Included studies proved a resting period that could be beneficial for recovery of median nerve though time of resting required values of variables to be back to baseline varied within studies. Additional problem raised on the consideration of the effect of time in the recovery phase could be addressed by future study.

# 4.4. Inclusion of symptomatic subjects

Our findings showed a controversial result on whether significant differences existed between symptomatic and asymptomatic subjects. To eliminate the probable effect of the presence of symptoms, two groups should be assessed independently. Suggested by some reviewed studies that there may be already certain level of restrictive movement of median nerve within carpal tunnel in individuals with the presence of symptoms.<sup>24</sup> The negative results may be caused by the difference in pathological changes of median nerve between the symptomatic group of different studies.

Table 3							
Sonographic	Sonographic scanning protocols						
Authors	CSA	æ	SR	Other measurements			
Impink et al. <sup>22</sup> Lai et al. <sup>23</sup>	Pisiform, distal radius Pisiform	Pisiform, radius Pisiform	Pisiform, radius				
Impink et al. <sup>24</sup> Toosi et al. <sup>25</sup>	Hamate, pisiform, radius Pisiform	Hamate, pisiform, radius Pisiform	Pisiform, radius Not mentioned				
Shim <sup>26</sup>	Proximal carpal tunnel region			Circumference: proximal carpal tunnel region	TH: proximal carpal tunnel region	BH: proximal carpal tunnel region	
Toosi et al. <sup>27</sup>	Pisiform, distal radius	Pisiform	Pisiform, radius				
Inal et al. <sup>28</sup>				Median nerve ratio: entrance of the carpal tunnel			
Hogaboom et al.29	Pisiform, radius		Pisiform, radius				
Loh et al. <sup>30</sup>	Proximal border of pisiform			D1: proximal border of pisiform	D2: proximal border of pisiform		
Woo et al. <sup>31</sup>	Outlet, inlet, proximal to inlet, distal radius, 4cm proximal to	Outlet, inlet, proximal to inlet, distal radius, 4-cm proximal		Circularity: outlet, inlet, proximal to inlet, distal radius, 4-cm proximal to	Perimeter: outlet, inlet, proximal to inlet, distal radius, 4-cm proximal to	TCL bulge: outlet, inlet	TCL thickness: outlet, inlet
	distal wrist crease	to distal wrist crease		distal wrist crease	distal wrist crease		
Rania et al. <sup>32</sup>	Level of carpal tunnel						
BH = bottom point of nerve; TCL = transve	BH = bottom point of median nerve to the lunate; CSA = cross-sectional area of median ner nerve; TCL = transverse carpal ligament; TH = highest point of median nerve to the lunate.	sectional area of median nerve; D1 = median nerve to the lunate.	edian nerve diameter in ra	dial-ulhar direction; D2 = median nerve diameter	BH = bottom point of median nerve to the lunate; CSA = cross-sectional area of median nerve; D1 = median nerve diameter in radial-ulnar direction; D2 = median nerve diameter in dorsal-palmar direction; FR = flattening ratio of median nerve; SR = swelling ratio of median nerve; TL = transverse carpal ligament; TH = highest point of median nerve to the lunate.	median nerve; SR = swellin	g ratio of median

#### 4.5. Effect of hand dominance

Hand movements in daily life are frequently demonstrated by the dominant side. There may be potential physiological changes resulted by daily tasks. The effect of activity may be exaggerated at the dominant hand. Adoption of bilateral scans occupied the greatest number of studies from our findings. Significant differences were also shown between left and right hands. Moreover, hand dominance was independently correlated to left-hand and right-hand CTS showed by a study.<sup>21</sup> The effect of hand dominance was proved to values of parameters. These findings may suggest bilateral scan of wrist serve as a more comprehensive measure for progression of CTS.

#### 4.6. Limitations of the included studies

In addition to the valuable findings from the studies, several limitations were noticed in their methodology that may draw questions to the results. Due to the user-dependent nature of ultrasonography, one reviewed study faced obstacles in obtaining image at certain location especially at the hamate level.<sup>24</sup> Thus, the study only included 30 subjects in the analysis of median nerve characteristics at the level. This may be insufficient to prove a significant result in terms of the proportion of subjects measured as mentioned above. The subjects who were unable to measure the variable at the hamate level from may have a significantly different direction of change in values.

Moreover, a study claiming there were no significant differences of median nerve under sonographs explained the results with the minor pathological changes the median nerve had already undergone during the progress of chronic CTS.<sup>24</sup> However, the changes were not significant enough to show evidence on images. This was limited by degree of CTS primarily happening on individuals, which varied among people and difficult to rank to exclude certain participants.

A subject position with a neutral position of wrist, supinated forearm and 90° flexion of elbow with sitting should be adopted during the ultrasound scan. For those who aimed to discuss the effect of extension and flexion of wrist and fingers, variations could be made in number of angles measured at corresponding regions. CSA and SR with sufficient levels scanned had significance on deducing the association. Investigators should include at least these two parameters and obtain values at the entire median nerve for CSA. Trends of variables resulted should be compared with the related pathological changes of median nerve.

Postrest scan is beneficial to find out whether a recovery phase is useful to reduce effect of activity to developing CTS. Duration of resting required may be varied with nature of activity but not duration of performing activity. A study taking measurement at several time points of a longer resting period could be done to achieve the aim. An ideal length of resting should be suggested to the population to reduce population prevalence of CTS.

For the effect of presence of CTS symptoms, it is recommended to eliminate it by separated studies. Generally, study design should be carefully customized according to the physiological and anatomical characteristics of the activity performed. Certain pathological change would be positive or negative to different participants by the same duration of performing. Investigation on how hand and wrist activities with different physiological change during and the intensity of the activity may affect the median nerve should be done prior.

Bilateral hands should be included in the assessment of CTS with comparison of results between groups done separately according to sides. It is suggested taking measurement on the nondominant hand when a unilateral scan is preferred. In addition, recommendations by the investigators of included studies should be taken as a reference. Longitudinal study was suggested to track the long-term effect of median nerve.<sup>22,25</sup> However, longitudinal study requires

Authors	Subject characteristics correlations	Article findings/results	Parameter-wrelated points
Impink et al. <sup>22</sup>	No significant relationships between baseline median nerve variables (CSA, FR, SR) and subject characteristics (age, year of wheelchair use, weight, BMI)	CSA: decreased significantly at distal radius, insignificantly at pisiform	SR: measured at pisiform and distal radius
Lai et al. <sup>23</sup>		FR: no significant difference at pisiform and distal radius Suggest performing longitudinal study to track the long-term effect on median nerve and investigate postacute effects	CSA: at pisiform is usually enlarged FR: measured at distal radius and pisiform; not at hamate due to technical difficulties CSA: increased after 5-min rapid task due
			to swelling; decreased in another experiment of activity on wheelchair
Impink et al. <sup>24</sup>	Baseline CSA at radius: significant positive correlated to BMI	Female excluded as subjects	
	FR at hamate: significant positive correlated to age	No significant differences of median nerve under sonographs Different direction of change for symptomatic and asymptomatic subjects CSA: increased in symptomatic subjects CSA: decreased in asymptomatic subjects Decrease of CSA in asymptomatic subjects were due to nature of the activity No significant findings in post-acute period Post-acute effect may appear after a few hours after the activity	
		Only 30 subjects included in the analysis of median nerve characteristics at level of hamate	Unable to obtain images at hamate level
Toosi et al. <sup>25</sup>	Baseline CSA at pisiform: significant positive correlated to age	FR: caught up in non-dominant with dominant wrist	Nondominant hand assessed Subjects may have minor pathological changes (From cited article) Median nerve long axis/short axis ratio: Decreased in asymptomatic subjects after 3-h keyboarding No significant changes in symptomatic subjects
		<ul> <li>FR: significant difference between both hands at baseline</li> <li>FR: no significant differences after task</li> <li>CSA: increased gradually after task and only significant at 60 min in dominant side</li> <li>SR: increased gradually after task and only significant at 60 min in dominant side</li> <li>Suggest performing longitudinal study</li> <li>Suggest adding resting period</li> </ul>	FR: only taken at pisiform
Shim et al. <sup>26</sup>		CSA: decreased significantly at proximal carpal tunnel after playing with smartphone CSA: decreased while TH and BH increased significantly at the same time	
Toosi et al. <sup>27</sup>	Wrist circumference: moderately related to baseline CSA and SR Wrist circumference: related to BMI and gender	FR: no significant difference with time points or hand dominance SR and CSA: significant enlarged in 30-min and	SR = CSA at pisiformCSA at distal radius FR: changed proportionally in
	SR: negatively correlated with age	60-min typing CSA and SR: returned to baseline in 30 min after	two dimensions FR: was measured at pisiform
nal et al.28		60-min typing	Median nerve ratio = Dominant side -
Hogaboom et al. <sup>29</sup>	Baseline SR: inversely proportional to body weight	CSA: increased significantly at pisiform but not in SR nor CSA at distal radius	Nondominant sideNondominant side Only nondominant hand scanned

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Authors	Subject characteristics correlations	Article findings/results	Parameter-wrelated points
Loh et al. <sup>30</sup>		CSA: consistently increased with each typing time block than the baseline	Increase in CSA did not affect the change of median nerve diameters in both directions
		CSA: showed a decreasing trend in the recovery phase Only included young male subjects	
Woo et al.31		CSA: not significantly different only at 4-cm proximal to distal wrist crease	
		FR, perimeter and TCL bulge: significant enlarged at carpal tunnel inlet in intensive than non-intensive users	
		TCL bulge: significant difference at carpal tunnel inlet betweer intensive and nonintensive users in both hands	1
		TCL bulge: significant difference at carpal tunnel inlet and outlet between left and right hands for intensive and nonintensive users	
		FR: significant difference only at level proximal to carpal tunnel inlet between left and right hands for intensive and non-intensive users	
Rania et al.32		CSA: higher in one hand than both hands	

BH = bottom point of median nerve; BMI = body mass index; CSA = cross-sectional area of median nerve; FR = flattening ratio of median nerve; SR = swelling ratio of median nerve; TCL = transverse carpal ligament; TH = highest point of median nerve to the lunate.

a much longer duration and resources. Thus, repeated cross-sectional studies could be considered to give a pseudo-longitudinal study if limitations exist.<sup>50</sup> There is a reminder on the consideration of confounding factors when longitudinal study is conducted as they may have a more severe effect in extended period.

On the basis of qualitative results obtained from this review, it is concluded that several criteria may assemble a guidance to reach standardization of methodology to assess upper limb activity– associated CTS. That is to say, ultrasonography could be useful in the diagnosis of CTS mostly with the visualization of pathological changes. Values could be added if the study design is customized with merits and disadvantages of each measure balanced.

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#### REFERENCES

- 1. Werner RA, Andary M. Carpal tunnel syndrome: pathophysiology and clinical neurophysiology. *Clin Neurophysiol* 2002;**113**:1373–81.
- Atroshi I, Gummesson C, Johnsson R, Ornstein E, Ranstam J, Rosén I. Prevalence of carpal tunnel syndrome in a general population. *JAMA* 1999;282:153–8.
- Werner RA, Armstrong TJ. Carpal tunnel syndrome: ergonomic risk factors and intracarpal. *Phys Med Rehabil Clin N Am* 1997;8:555–69.
- Armstrong TJ, Castelli WA, Evans FG, Diaz-Perez R. Some histological changes in carpal tunnel contents and their biomechanical implications. *J Occup Med* 1984;26:197–201.
- de Krom MC, Kester AD, Knipschild PG, Spaans F. Risk factors for carpal tunnel syndrome. *Am J Epidemiol* 1990;132:1102–10.
- Armstrong T, Dale AM, Franzblau A, Evanoff BA. Risk factors for carpal tunnel syndrome and median neuropathy in a working population. J Occup Environ Med 2008;50:1355–64.
- Bugajska J, Jedryka-Góral A, Sudol-Szopińska I, Tomczykiewicz K. Carpal tunnel syndrome in occupational medicine practice. *Int J Occup* Saf Ergon 2007;13:29–38.

- Turner JA, Franklin G, Fulton-Kehoe D, Sheppard L, Wickizer TM, Wu R, et al. Early predictors of chronic work disability associated with carpal tunnel syndrome: a longitudinal workers' compensation cohort study. *Am J Ind Med* 2007;50:489–500.
- Harrington JM, Carter JT, Birrell L, Gompertz D. Surveillance case definitions for work related upper limb pain syndromes. Occup Environ Med 1998;55:264–71.
- Rizzello G, Longo UG, Franceschi F, Martinelli N, Meloni MC, Quadrini R, et al. Compression neuropathy of the motor fibers of the median nerve at wrist level. J Chin Med Assoc 2009;72:268–70.
- 11. Jablecki CK, Andary MT, Floeter MK, Miller RG, Quartly CA, Vennix MJ, et al; American Association of Electrodiagnostic Medicine; American Academy of Neurology; American Academy of Physical Medicine and Rehabilitation. Practice parameter: Electrodiagnostic studies in carpal tunnel syndrome. Report of the American Association of Electrodiagnostic Medicine, American Academy of Neurology, and the American Academy of Physical Medicine and Rehabilitation. *Neurology* 2002;58:1589–92.
- Buchberger W, Schön G, Strasser K, Jungwirth W. High-resolution ultrasonography of the carpal tunnel. J Ultrasound Med 1991;10:531–7.
- 13. Duncan I, Sullivan P, Lomas F. Sonography in the diagnosis of carpal tunnel syndrome. *AJR Am J Roentgenol* 1999;173:681–4.
- Beekman R, Visser LH. Sonography in the diagnosis of carpal tunnel syndrome: a critical review of the literature. *Muscle Nerve* 2003;27:26–33.
- Middleton WD, Kneeland JB, Kellman GM, Cates JD, Sanger JR, Jesmanowicz A, et al. MR imaging of the carpal tunnel: normal anatomy and preliminary findings in the carpal tunnel syndrome. *AJR Am J Roentgenol* 1987;148:307–16.
- Impink BG, Gagnon D, Collinger JL, Boninger ML. Repeatability of ultrasonographic median nerve measures. *Muscle Nerve* 2010;41:767–73.
- Hobson-Webb LD, Padua L. Ultrasound of Focal Neuropathies. J Clin Neurophysiol 2016;33:94–102.
- Descatha A, Huard L, Aubert F, Barbato B, Gorand O, Chastang JF. Meta-analysis on the performance of sonography for the diagnosis of carpal tunnel syndrome. *Semin Arthritis Rheum* 2012;41:914–22.
- Torres-Costoso A, Martínez-Vizcaíno V, Álvarez-Bueno C, Ferri-Morales A, Cavero-Redondo I. Accuracy of ultrasonography for the diagnosis of carpal tunnel syndrome: a systematic review and meta-analysis. *Arch Phys Med Rehabil* 2018;99:758–65.e10.
- Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al; PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4:1.
- Wohlin C. Proceedings of the 18th International Conference on Evaluation and Assessment in Software Engineering, May 2014; London, United Kingdom, 1–10.
- Impink BG, Boninger ML, Walker H, Collinger JL, Niyonkuru C. Ultrasonographic median nerve changes after a wheelchair sporting event. Arch Phys Med Rehabil 2009;90:1489–94.

- Lai WK, Chiu YT, Law WS. The deformation and longitudinal excursion of median nerve during digits movement and wrist extension. *Man Ther* 2014;19:608–13.
- 24. Impink BG, Collinger JL, Boninger ML. The effect of symptoms of carpal tunnel syndrome on ultrasonographic median nerve measures before and after wheelchair propulsion. *PM R* 2011;3:803–10.
- Toosi KK, Impink BG, Baker NA, Boninger ML. Effects of computer keyboarding on ultrasonographic measures of the median nerve. Am J Ind Med 2011;54:826–33.
- Shim JM. The effect of carpal tunnel changes on smartphone users. J Phys Ther Sci 2012;24: 1251–3.
- 27. Toosi KK, Hogaboom NS, Oyster ML, Boninger ML. Computer keyboarding biomechanics and acute changes in median nerve indicative of carpal tunnel syndrome. *Clin Biomech (Bristol, Avon)* 2015;30: 546-50.
- Inal EE, DemIrcI k, Çetİntürk A, Akgönül M, Savaş S. Effects of smartphone overuse on hand function, pinch strength, and the median nerve. *Muscle Nerve* 2015;52:183–8.
- 29. Hogaboom NS, Diehl JA, Oyster ML, Koontz AM, Boninger ML. Ultrasonographic median nerve changes after repeated wheelchair transfers in persons with paraplegia: relationship with subject characteristics and transfer skills. *PM R* 2016;8:305–13.
- Loh PY, Yeoh WL, Nakashima H,Muraki S. Impact of keyboard typing on the morphological changes of the median nerve. J Occup Health 2017:17-0058-OA.
- Woo EHC, White P, Lai CWK. Effects of electronic device overuse by university students in relation to clinical status and anatomical variations of the median nerve and transverse carpal ligament. *Muscle Nerve* 2017;56:873–80.
- Rania R, Mousa ME, Khaled A, Marwa Sh, Mostafa S. Effect of bilateral versus unilateral use of smartphone on cross sectional area of median nerve. *Med J Cairo Univ* 2019;87:2201–5.
- 33. Zambelis T, Tsivgoulis G, Karandreas N. Carpal tunnel syndrome: associations between risk factors and laterality. *Eur Neurol* 2010;63:43–7.
- Werner RA, Albers JW, Franzblau A, Armstrong TJ. The relationship between body mass index and the diagnosis of carpal tunnel syndrome. *Muscle Nerve* 1994;17:632–6.
- Boz C, Ozmenoglu M, Altunayoglu V, Velioglu S, Alioglu Z. Individual risk factors for carpal tunnel syndrome: an evaluation of body mass index, wrist index and hand anthropometric measurements. *Clin Neurol Neurosurg* 2004;106:294–9.
- McLellan DL, Swash M. Longitudinal sliding of the median nerve during movements of the upper limb. J Neurol Neurosurg Psychiatry 1976;39:566-70.

- Nanno M, Sawaizumi T, Kodera N, Tomori Y, Takai S. Transverse ultrasound assessment of the displacement of the median nerve in the carpal tunnel during wrist and finger motion in healthy volunteers. J Nippon Med Sch 2015;82:170–9.
- Wang Y, Filius A, Zhao C, Passe SM, Thoreson AR, An KN, et al. Altered median nerve deformation and transverse displacement during wrist movement in patients with carpal tunnel syndrome. *Acad Radiol* 2014;21:472–80.
- Echigo A, Aoki M, Ishiai S, Yamaguchi M, Nakamura M, Sawada Y. The excursion of the median nerve during nerve gliding exercise: an observation with high-resolution ultrasonography. *J Hand Ther* 2008;21:221–7; quiz 228.
- Dilley A, Lynn B, Greening J, DeLeon N. Quantitative in vivo studies of median nerve sliding in response to wrist, elbow, shoulder and neck movements. *Clin Biomech (Bristol, Avon)* 2003;18:899–907.
- Yucel A, Yaman M, Acar M, Haktanir A, Albayrak R, Degirmenci B. Sonographic findings of median nerve and prevalence of carpal tunnel syndrome in computer mouse users. *Neuroradiol J* 2005;18:212–20.
- 42. Klauser AS, Halpern EJ, De Zordo T, Feuchtner GM, Arora R, Gruber J, et al. Carpal tunnel syndrome assessment with US: value of additional cross-sectional area measurements of the median nerve in patients versus healthy volunteers. *Radiology* 2009;**250**:171–7.
- Mallouhi A, Pülzl P, Pültzl P, Trieb T, Piza H, Bodner G. Predictors of carpal tunnel syndrome: accuracy of gray-scale and color Doppler sonography. *AJR Am J Roentgenol* 2006;186:1240–5.
- Walker FO, Cartwright MS, Wiesler ER, Caress J. Ultrasound of nerve and muscle. Clin Neurophysiol 2004;115:495–507.
- 45. Yoon JS, Hong SJ, Kim BJ, Kim SJ, Kim JM, Walker FO, et al. Ulnar nerve and cubital tunnel ultrasound in ulnar neuropathy at the elbow. *Arch Phys Med Rehabil* 2008;89:887–9.
- Buchberger W, Judmaier W, Birbamer G, Lener M, Schmidauer C. Carpal tunnel syndrome: diagnosis with high-resolution sonography. *AJR Am J Roentgenol* 1992;159:793–8.
- Keberle M, Jenett M, Kenn W, Reiners K, Peter M, Haerten R, et al. Technical advances in ultrasound and MR imaging of carpal tunnel syndrome. *Eur Radiol* 2000;10:1043–50.
- Altinok MT, Baysal O, Karakas HM, Firat AK. Sonographic evaluation of the carpal tunnel after provocative exercises. J Ultrasound Med 2004;23:1301–6.
- Marquardt TL, Gabra JN, Li ZM. Morphological and positional changes of the carpal arch and median nerve during wrist compression. *Clin Biomech (Bristol, Avon)* 2015;30:248–53.
- 50. Levin KA. Study design III: cross-sectional studies. *Evid Based Dent* 2006;7:24-5.