Ultrasonographic Assessment of Carpal Tunnel Syndrome Severity

A Systematic Review and Meta-Analysis

Peyman Roomizadeh, MD, Bina Eftekharsadat, MD, Amin Abedini, MD, Sepideh Ranjbar-kiyakalayeh, MD, Naseh Yousefi, MD, Safoora Ebadi, PhD, and Arash Babaei-Ghazani, MD

Objective: The aim of the study was to investigate the overall estimates of cross-sectional areas of the median nerve measured by ultrasonography in accordance with the electrodiagnostic classification of carpal tunnel syndrome severity.

Design: MEDLINE (PubMed), Embase (Ovid), and Web of Science were searched for studies reporting the median nerve cross-sectional area measured by ultrasonography for mild, moderate, and severe carpal tunnel syndrome based on electrodiagnostic study. Cross-sectional area values measured at the carpal tunnel inlet were included in the analyses.

Results: Overall, 866 citations were retrieved and checked for eligibility. Finally, 16 articles were included for meta-analysis. These studies included a total sample of 2292 wrists including 776 mild, 823 moderate, and 693 severe carpal tunnel syndrome. The pooled analysis revealed a mean cross-sectional area of 11.64 mm^2 (95% confidence interval = 11.23–12.05 mm^2, $P < 0.001$) for mild carpal tunnel syndrome, a mean cross-sectional area of 13.74 mm^2 (95% confidence interval = 12.59–14.89 mm^2, $P < 0.001$) for moderate carpal tunnel syndrome, and a mean cross-sectional area of 16.80 mm^2 (95% confidence interval = 14.50–19.1 mm^2, $P < 0.001$) for severe carpal tunnel syndrome.

Conclusions: This is the first meta-analysis that provides the pooled median nerve cross-sectional area values in accordance with the electrodiagnostic classification of carpal tunnel syndrome severity. The values obtained in this study have clinical utility in ultrasonographic assessment of patients with carpal tunnel syndrome.

Key Words: Carpal Tunnel Syndrome, Ultrasonography, Electrodiagnosis, Diagnosis, Review, Meta-analysis

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Carpal tunnel syndrome (CTS) is the most common peripheral compression neuropathy of the median nerve in the upper limb. Depending on the criteria used for diagnosis, the prevalence has been reported to vary from 3% to 6% in the general population. There is a 3:1 female predominance with a mean age of onset in the early 40s.[1–3] The classic presentation is numbness and pain in the first three radial digits and the radial side of the forth finger corresponding to the innervation of the median nerve in the hand. The diagnosis is based primarily on clinical features, but electrodiagnostic studies are widely used to confirm the diagnosis and determine the stage of severity.[4,5]

During the last decade, high-frequency ultrasonography is extensively being used in the field of neuromusculoskeletal medicine. One major application is evaluation of peripheral nerve entrapments in the upper and lower limbs. The most reliable ultrasonographic indicator of peripheral nerve entrapment neuropathy is enlargement of the nerve cross-sectional area (CSA).[6] Many studies have compared the diagnostic yields of ultrasonography versus electrodiagnostic studies in patients with CTS. There is now mounting evidence that ultrasonography can be used as an alternative to electrodiagnostic studies in the diagnosis of CTS.[7,8] A median nerve CSA 10 mm^2 or greater at the level of the pisiform bone is the most consistent parameter for diagnosis of CTS by ultrasonography. The diagnostic sensitivity has been estimated to be as high as 97% using this parameter.[9,10] Several studies have attempted to discover whether the CSA of the median nerve is useful for predicting the severity of median neuropathy as determined by nerve conduction studies or not. In recent years, increasing numbers of authors have provided data on the mean CSA of the median nerve in accordance with electrophysiological grading of CTS severity. However, the existing published data need to be consolidated into a full meta-analysis to determine the overall estimate of median nerve CSAs for mild, moderate, and severe CTS.

The purpose of this study was to conduct a meta-analysis on high-quality research to determine the overall estimates of median nerve CSA at carpal tunnel inlet for mild, moderate, and severe CTS as defined by the electrodiagnostic studies.

MATERIALS AND METHODS

This systematic review was conducted in accordance with the Cochrane Collaboration guidelines[11] and the Preferred

From the Neuromusculoskeletal Research Center, Department of Physical Medicine and Rehabilitation, Iran University of Medical Sciences, Tehran, Iran (PR, NY, SE, AB-G); Physical Medicine and Rehabilitation Research Center, Tabriz University of Medical Sciences, Tabriz, Iran (BE, SR); and Medical Students Research Center, Isfahan University of Medical Sciences, Isfahan, Iran (AA).

All correspondence should be addressed to: Arash Babaei-Ghazani, MD, Neuromusculoskeletal Research Center, Department of Physical Medicine and Rehabilitation, Firozgar Hospital, Valieasr Sq, Tehran, Iran.

Peyman Roomizadeh is in training.

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Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement (Supplemental Digital Content 1, http://links.lww.com/PHM/A709).[12] This study was exempt from ethical approval because it was a secondary analysis of a publicly available datasets.

Sources and Search Strategy

In December 2017, two authors (PR and SR) independently conducted a systematic search of MEDLINE (PubMed), EMBASE (Ovid), and Web of Science to identify relevant publications from the inception of the databases to December 1, 2017, without any restrictions. The following text words, Medical Subject Headings (MeSH) terms, and Boolean operators were used: "carpal tunnel or carpal tunnel syndrome or median nerve", "electrodiagnostic or electrophysiologic or electrodiagnostically or electromyography or nerve conduction or neurophysiologic", and "ultrasound or ultrasonography or ultrasonographic, sonography or sonographic or sonographically." The search was conducted without any language restriction.

Inclusion and Exclusion Criteria

The titles and abstracts of all collected studies were reviewed for relevance by the same authors (PR and SR). Disagreements were resolved through discussion to a third author (AB) when necessary. The criteria for study inclusion in this systematic review were as follows: (*a*) study performing both high-frequency ultrasonography and electrodiagnostic study of the median nerve in patients with CTS; (*b*) study reporting the median nerve CSA for mild, moderate, and severe CTS in accordance with electrodiagnostic studies; (*d*) clearly described electrodiagnostic grading scale for defining the severity of CTS, and (*e*) study published in full text. We did not include case reports, case series, letters, review articles, technical reports, and conference abstracts in this systematic review. The primary reason for not including some relevant articles was lack of describing valid electrodiagnostic criteria for defining mild, moderate, and severe CTS. The eligible studies that met the inclusion criteria were imported into EndNote software Version X7 (Thomson Reuters, Carlsbad, CA).

Quality Assessment

We evaluated the scientific quality of the studies using the "STrengthening the Reporting of Observational Studies in Epidemiology" (STROBE) tool[13] (see Supplementary Checklist, Supplemental Digital Content 2, http://links.lww.com/PHM/A710). The STROBE is a standard international checklist for quality assessment of the observational studies including cohort studies, case-control studies, and cross-sectional studies. This tool evaluates components of the study design, methods for selecting participants, data collection, methods for measuring exposure and outcome variables, statistical methods, potential bias, and methods to control for confounding. Studies with STROBE score of less than 8 were not included in the meta-analysis. Two authors (PR and AA) performed the quality assessment separately and disagreements were resolved through discussion.

Data Extraction and Outcome Measures

After enrollment of the eligible studies, one author (SR) extracted data from each article including the name of the first author, year of publication, number of patients, number of median nerves examined (number of wrists), mean age of the studied sample, sex ratio, and mean ± standard deviation (SD) of the median nerve CSA corresponding to mild, moderate, and severe CTS. The extracted data were summarized into standard data tables designed for this review. For studies that reported various median nerve CSA measurements at different anatomical sites, we only included the median nerve CSAs measured at the level of pisiform bone (carpal tunnel inlet) in this analyses.

Because no generally accepted electrophysiological scale for grading the severity of CTS has been reached yet, studies included in the present review applied four different grading scales. These scales are derived from the publications by Steven,[14] Padua et al.,[15] Bland,[16] and Sucher.[17] The details of these grading schemes are given in Table 1. The Steven and Sucher scales use three grades as "mild," "moderate," and "severe," with a relatively similar electrophysiological criteria. The Padua and the Bland scales divide the mild and the severe grades into more subgroups, and use five and six grades, respectively. To conduct the meta-analysis, we grouped the Bland and the Padua scales into the following three grades:

Mild CTS: Bland grade 1 (very mild) and grade 2 (mild); Padua grade 1 (minimal) and grade 2 (mild).

Moderate CTS: Bland grade 3 (moderate); and Padua grade 3 (moderate).

Severe CTS: Bland grade 4 (severe), grade 5 (very severe) and grade 6 (extremely severe); and Padua grade 4 (severe) and grade 5 (extreme).

Data Synthesis

The pooled means of CSA in mild, moderate, and severe CTS and their 95% confidence intervals (CI) were evaluated using random-effects models. The pooled CSAs were synthesized by considering the means of each study weighted by its sample size (number of wrists) for mild, moderate, and severe CTS. χ^2 tests and I^2 statistics were used to evaluate the heterogeneity between the studies. In the χ^2 test, when the P value of Cochran's Q was lower than 0.1, the heterogeneity was considered.[18,19] The results of I^2 test were interpreted as follows: (*a*) 0%–40% might not be important, (*b*) 30%–60% might represent moderate heterogeneity, (*c*) 50%–90% might represent substantial heterogeneity, and (*d*) 75%–100% might indicate considerable heterogeneity.[11,19] When heterogeneity between studies was detected, a leave-one-out sensitivity analysis was conducted by sequentially removing one study at a time and recalculating the results to assess the consistency of the results. To assess the publication bias, Funnel plots, Begg's test, and Egger's regression model were used.[20,21] When publication bias was detected, trim and fill method was used to adjust the results. All statistical analysis were performed using Comprehensive Meta-Analysis Software Version 3 (Biostat Inc, Englewood, NJ).

RESULTS

Eligibility of Studies

A total of 866 citations were identified by our initial search. Of these, 842 studies were excluded based on the title

TABLE 1. Electrophysiological grading scales for the severity of carpal tunnel syndrome

Steven classification[14]:
- **Mild:** Prolonged DSL or MNL ± SNAP amplitude below the lower limit of normal.
- **Moderate:** Abnormal median DSL as above, and prolonged median DML.
- **Severe:** Prolonged median DSL and DML with either an absent SNAP or mixed nerve action potentials, or low amplitude or absent thenar CMAP. Evidence of membrane instability, reduced recruitment, and motor unit potential changes in EMG.

Padua classification[15]:
- **Minimal (grade 1):** Abnormal segmental or comparative tests only.
- **Mild (grade 2):** Slowing of digit/wrist sensory nerve conduction velocity with normal DML.
- **Moderate (grade 3):** Slowing of digit/wrist sensory nerve conduction velocity with abnormal DML.
- **Severe (grade 4):** Absence of SNAP and abnormal DML.
- **Extreme (grade 5):** Absent SNAP and CMAP.

Bland classification[16]:
- **Very mild (grade 1):** CTS demonstrable only with most sensitive tests.
- **Mild (grade 2):** Slow of digit/wrist sensory nerve conduction velocity with normal DML.
- **Moderate (grade 3):** SNAP amplitude preserved with DML < 6.5 millisecs.
- **Severe (grade 4):** SNAP amplitude absent but CMAP amplitude preserved, DML < 6.5 millisecs.
- **Very severe (grade 5):** DML > 6.5 millisecs with recordable CMAP amplitude.
- **Extremely severe (grade 6):** Absent SNAP and CMAP.

Sucher classification[17]:
- **Mild:** Prolonged DSL and/or median MNL, and Normal or minimally prolonged DML, and Amplitudes of all responses within normal range, and No CB or mild CB, and No thenar EMG abnormalities.
- **Moderate:** Prolonged DSL, MNL, and DML, and Amplitudes of all tested responses may be diminished, typically a relative decrease, and CB may be present, and Minor thenar EMG abnormalities may be present.
- **Severe:** Unobtainable median SNAP (or low amplitude and very prolonged DSL), and Low-amplitude or unobtainable median mixed nerve response and, if present, very prolonged MNL, and Low-amplitude or unobtainable median CMAP and, if present, very prolonged DML, and CB may be present and pronounced, and Thenar EMG abnormalities often present.

CB, conduction block; CMAP, compound muscle action potential; DML, distal motor latency; DSL, distal sensory latency; EMG, electromyography; MNL, mixed nerve latency; SNAP, sensory nerve action potential.

and abstract screening because they were irrelevant studies, duplicates, case reports, case series, letters, review articles, conference abstracts, and technical reports. Twenty-four relevant studies were selected and their full texts were obtained for further assessments. On further scrutiny, eight studies were excluded from the meta-analysis primarily because of not describing a definite electrodiagnostic grading scale for defining mild, moderate, and severe CTS. Finally, 16 studies with appropriate quality met the inclusion criteria for this meta-analysis.[22–37] No additional citations were identified in searching the reference lists of the included studies. A summary of the searching strategy and selection process is illustrated in Figure 1.

The included studies were all written in English language and were published from 2004 to 2017. They were all cross-sectional studies. These studies included a total sample of 2292 wrists including 776 mild, 823 moderate, and 693 severe CTS. Table 2 demonstrates the main characteristics of the 16 included studies.

Quantitative Synthesis

Heterogeneity was observed across the studies in the means of CSA in all groups of mild, moderate, and severe CTS. The details of heterogeneity analysis (I^2 statistics) are described in Table 3. Accordingly, the random-effect models were used to pool the data. The pooled analysis revealed a mean CSA of 11.64 mm^2 (95% CI = 11.23–12.05 mm^2, $P < 0.001$) for mild CTS (Fig. 2), a mean CSA of 13.74 mm^2 (95% CI = 12.59–14.89 mm^2, $P < 0.001$) for moderate CTS (Fig. 3), and a mean CSA of 16.80 mm^2 (95% CI = 14.50–19.1 mm^2, $P < 0.001$) for severe CTS (Fig. 4). Among the included studies in the meta-analysis, 12 studies[22–29,31,33,35,36] reported the median nerve CSA for normal healthy volunteers/control subjects. The pooled analysis revealed a mean CSA of 8.21 mm^2 (95% CI = 8.03–8.38 mm^2, $P < 0.001$) for normal median nerves.

Sensitivity Analysis

To evaluate the consistency of the results, a leave-one-out sensitivity analysis was performed by sequentially excluding one study at a time and recalculating the pooled means repeatedly. The sensitivity analysis revealed no significant change in the pooled means of CSA in all three severity grades of CTS when all studies were excluded one by one. This indicated the robustness and stability of the results.

Publication Bias Analysis

The results of Funnel plots, Begg's test, and Egger's tests revealed publication bias in the means of CSAs in moderate and severe CTS (Table 4). To address the issue of publication bias, we performed trim and fill analysis to adjust the means of CSAs in moderate and severe CTS. The adjusted means for moderate and severe CTS were 13.43 mm^2

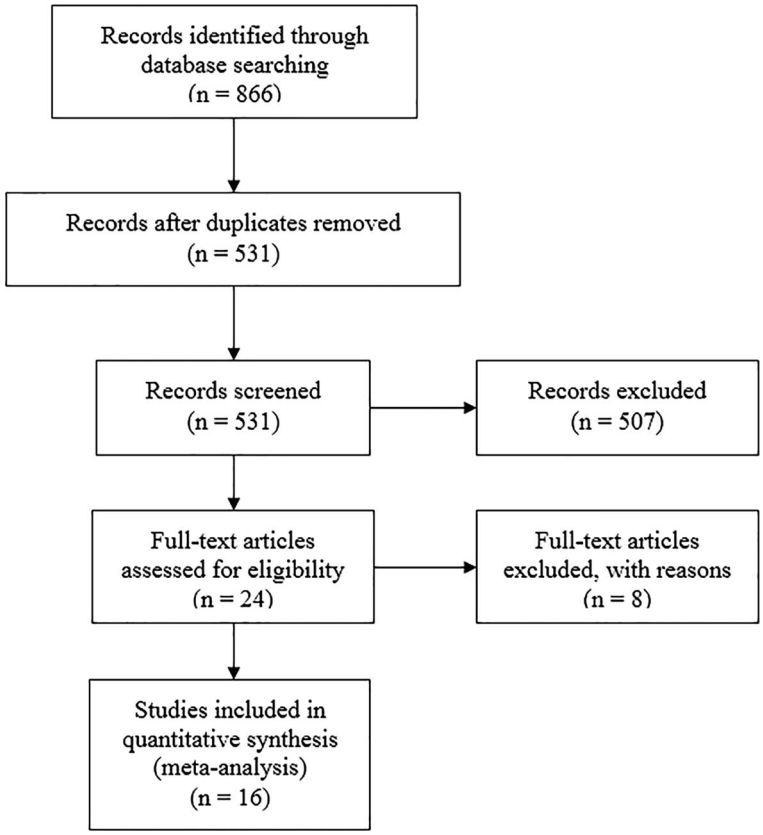

FIGURE 1. Flow diagram for inclusion of the studies in the meta-analysis.

(95% CI = 11.68–15.17 mm^2) and 16.36 mm^2 (95% CI = 13.52–19.2 mm^2), respectively.

DISCUSSION

One of the main reasons for carrying out electrodiagnostic study in CTS is to assess the severity of the median neuropathy at the wrist. Many electrophysiological grading schemes exist for describing the severity of the CTS. These methods generally rely on measuring the degree of nerve conduction slowing across the carpal tunnel or determining whether sensory or motor action potentials are present. However, most available grading schemes are arbitrary in nature.[17] The variety of grading schemes means that there is no universally accepted electrophysiological scale for grading the severity of CTS. The most commonly used scales are derived from the publications by Steven,[14] Padua et al.,[15] and Bland[16] (Table 1). Steven's used three grades as "mild," "moderate," and "severe" but did not specify latency levels within each grade. Padua et al.[15] suggested a five-grading scheme very similar to that of Steven's scale, the difference being that it divides mild CTS into "minimal" and "mild" subdivisions and severe CTS into "severe" and "extreme" subdivisions. They did not specify latency levels within each grade as well. Finally, Bland used six grades and determined specific latency cutoffs for each grade (Table 1). These scales can be mapped onto each other to some extent, with Bland providing the greatest number of subdivisions, then Padua and then Stevens. In 2013, Sucher[17] proposed a new grading scheme based on a combination of the ranking criteria used in previous publications by Bland,[16] Stevens,[14] and Padua.[15] This scheme uses three grades as mild, moderate, and severe and is suggested to be a nonarbitrary means of determining CTS severity. Although there are only slight variations between these grading scales, the controversy about classifying patients into mild, moderate, and severe CTS is probably the most important challenge for the research of CTS severity in general. However, to conduct the present meta-analysis, we grouped the Bland grades 1 and 2 (very mild, mild) and Padua grades 1 and 2 (minimal, mild) into "mild CTS." Similarly, we grouped the Bland grades 4 to 6 (severe, very severe, and extremely severe) and Padua grades 4 and 5 (severe, extreme) into "severe CTS."

In this systematic review and meta-analysis, we incorporated 16 studies assessing the median nerve CSA at the carpal tunnel inlet in accordance with the electrophysiological classifications of CTS severity. Based on findings of this study, the pooled results of the exiting literature for median nerve CSA was 11.64 mm^2 for mild, 13.74 mm^2 (adjusted: 13.43 mm^2) for moderate, and 16.80 mm^2 (adjusted: 16.36 mm^2) for severe CTS. To our knowledge, this is the first meta-analysis that provides the pooled median nerve CSA values in accordance with the electrodiagnostic classification of CTS severity. The values obtained in this study have clinical utility in ultrasonographic assessment of patients with CTS.

Increased nerve CSA is an important diagnostic finding in compression neuropathies.[6] Prolonged compression of the nerve will result in changes in the neural microcirculation and render the nerve susceptible to ischemia. Nerve ischemia is responsible for blood vessel endothelial permeability

TABLE 2. Characteristics of the included studies

Author, Year	No. Patients	No. Wrists	Age, y	Sex (F:M)	No. Mild CTS	No. Moderate CTS	No. Severe CTS	Location of CSA Measurement	CSA, Mean ± SD, mm^2		
									Mild CTS	Moderate CTS	Severe CTS
El Miedany et al., 2004[22]	78	90	44.9 ± 6.16	51:27	30	33	27	Inlet	11.7 ± 0.2	16.7 ± 0.3	20.7 ± 0.1
Mohammadi et al., 2010[23]	82	132	43.6 ± 9	74:8	34	53	45	Inlet	10.8 ± 1.9	11.4 ± 1.8	12.0 ± 1.5
Karadag et al., 2010[24]	NA	50	43.3 ± 11	NA	24	18	8	Inlet	11.73 ± 1.84	13.98 ± 2.74	16.34 ± 2.96
Mohammadi et al., 2012[25]	60	90	45.2	52:8	28	33	29	Inlet	11.07 ± 2.08	11.73 ± 1.56	12.59 ± 1.7
Kang et al., 2012[26]	110	110	NA	100:10	28	46	36	Inlet	13.51 ± 3.72	14.67 ± 2.93	18.74 ± 6.01
Yazdchi et al., 2012[27]	90	155	48.52 ± 12.17	68:22	34	99	22	Inlet	11.41 ± 2.56	12.40 ± 4.01	15.10 ± 4.74
								Outlet	10.47 ± 2.20	11.25 ± 3.29	13.86 ± 4.04
Ajeena et al., 2013[28]	35	63	41.5 ± 6.5	35:00	25	27	11	Inlet	10.26 ± 0.83	13.81 ± 1.62	17.86 ± 1.89
Sarraf et al., 2013[29]	38	71	47.1 ± 10.9	NA	21	37	13	Inlet	12.7 ± 3.3	14.3 ± 5.3	15.1 ± 3.8
Abrishamchi et al., 2014[30]	52	81	51.8 ± 10.8	45:7	26	32	23	Inlet	12.0 ± 3.0	15.0 ± 3.0	19.0 ± 6.0
Kim et al., 2014[31]	NA	246	53.0	NA	66	91	89	Inlet	11.5 ± 2.3	13.1 ± 3.8	15.8 ± 4.8
Kwon et al., 2014[32]	50	92	55.6 ± 8.1	45:5	23	30	39	Inlet	10.5 ± 4.6	11.6 ± 2.6	17.1 ± 7.5
Azami et al., 2014[33]	90	120	56.8 ± 10.6	83:7	57	29	34	Inlet	10.66 ± 0.8	13.79 ± 0.82	17.35 ± 2.62
								Outlet	9.38 ± 1.43	11.80 ± 0.91	13.46 ± 1.87
Klauser et al., 2015[34]	427	643	57.9 ± 14.7	325:102	272	152	219	Inlet	12.52 ± 2.74	14.66 ± 2.50	18.81 ± 5.31
Ghasemi et al., 2015[37]	52	81	51.8 ± 10.8	45:7	26	32	23	Inlet	12.0 ± 3.0	15.0 ± 3.0	19.0 ± 6.0
Borire et al., 2016[35]	NA	131	NA	NA	49	41	41	Inlet	13.2 ± 3.5	14.0 ± 3.0	18.2 ± 6.2
Phongamwong et al., 2017[36]	106	137	53.1 ± 12.8	87:19	33	70	34	Inlet	12.0 ± 2.7	13.8 ± 4.7	15.4 ± 4.1

Data are presented as numbers or mean ± SD.

F, females; M; males; NA, not available.

TABLE 3. Heterogeneity in studies

Parameters	*Q*	*df* (*Q*)	*P*	I^2
Mild CTS	212.76	15	0.000	92.95
Moderate CTS	1329.161	15	0.000	98.87
Severe CTS	2486.884	15	0.000	99.39

abnormalities, which can lead to intraneural edema. With increased compression, there will be intrafascicular edema, fibrous tissue proliferation, and higher proportion of extracellular water contents in the affected nerve. These structural changes result in swelling of the nerve, which is reflected by increased nerve CSA in ultrasound examination.[6,8,9] The associations between CTS severity and median nerve CSA have been demonstrated in several studies. In a study on 106 patients with moderate to severe CTS, Phongamwong et al.[36] reported a significant positive correlation ($r = 0.56$) between CTS severity and median nerve CSA measured at carpal tunnel inlet. Using receiver operator characteristics analysis, they showed that a cutoff value of 14 mm^2 for median nerve CSA has 91.4% specificity and 42.3% sensitivity to rule in moderate to severe CTS. This cutoff value is very close to the pooled estimates of 13.74 mm^2 for moderate CTS obtained in our meta-analysis. Padua et al.[38] made a similar observation and reported a correlation coefficient of 0.80 between median nerve CSA and electrodiagnostic classification of CTS severity. In another study, Karadag et al.[24] evaluated the agreements between the two methods of electrodiagnostic studies and ultrasonography in classification of CTS severity. They showed a good agreement (Cohen's κ coefficient = 0.619) between these two methods in classifying CTS as mild, moderate, and severe. Despite these promising reports, a number of authors including Moran et al.[39] and Mhoon et al.[40] have found no significant correlation between the values of the median nerve CSA and electrodiagnostic severity scales.

Ultrasonographic measurement of the median nerve CSA can be performed at the carpal tunnel inlet (the level of scaphoid-pisiform) or at the level of carpal tunnel outlet (the level of hamate-trapezium). All studies included in this meta-analysis performed ultrasound measurements at the carpal tunnel inlet. Measurement of median nerve CSA at the carpal tunnel inlet is reportedly more sensitive for diagnosis of CTS.[9,10] In addition, it has been shown that measurement of the median nerve CSA at the carpal tunnel inlet has a better interreader reliability than the measurements at the carpal tunnel outlet.[39,41] The poor interreader reliability at the carpal tunnel outlet may be explained by difficulty in visualizing the median nerve at this level, because the nerve moves more dorsally and is covered by a thick palmar skin.[9,37] However, it should be acknowledged that the ultrasonographic assessment of median nerve is highly dependent on the skill and expertise of the practitioner. The way that the operator performs the ultrasound examination may greatly affect the values of measured CSAs. Considerable expertise are required to perform ultrasonographic assessment of the median nerve for diagnosis of CTS.

Ultrasonography represents an emerging diagnostic technique to assess median neuropathy at wrist; it is an alternative to more traditional electrodiagnostic study. However, each technique has some advantages and some shortcomings. Ultrasonography provides real-time imaging of the carpal tunnel and allows dynamic evaluation of the median nerve and the surrounding structures. Imaging can be used for evaluating anatomic variations or possible compressing masses that may be responsible for median nerve compression. Furthermore, ultrasonography is noninvasive and requires a shorter examination time and lower costs than electrodiagnostic studies.[9] On the other hand, electrodiagnostic studies are more powerful in the assessment of differential diagnosis in individuals with symptoms that suggest CTS. For example, CTS often occurs in the context of a generalized peripheral polyneuropathy, for example, in the setting of diabetes mellitus. Electrodiagnostic study is able to

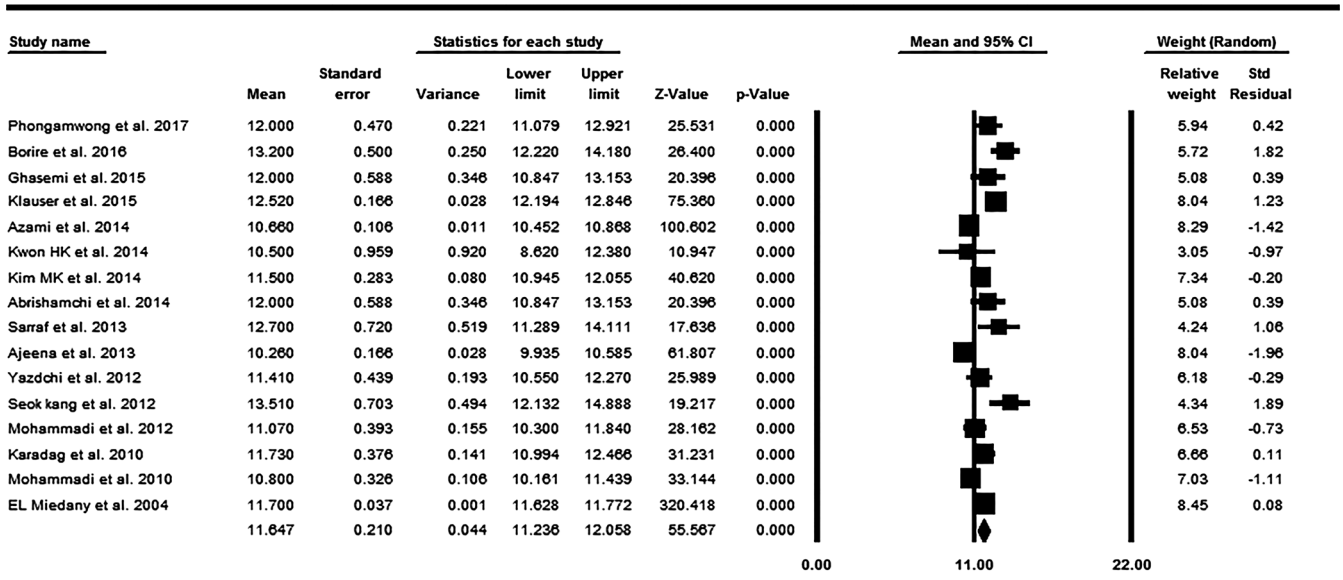

FIGURE 2. The forest plot of mean cross-sectional areas for mild CTS.

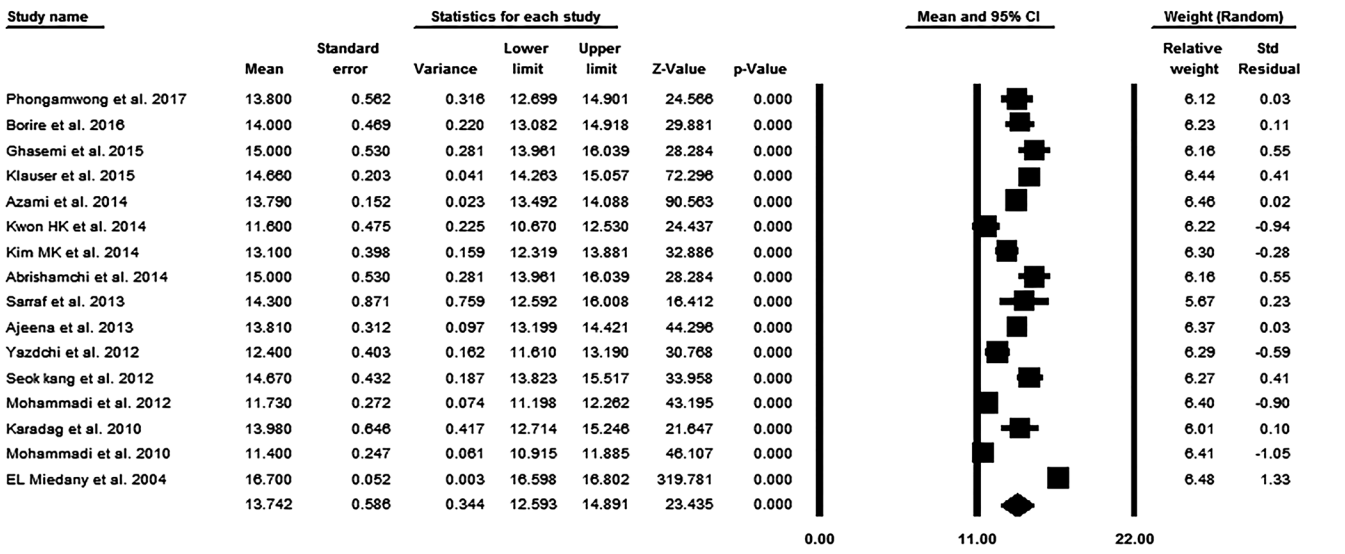

FIGURE 3. The forest plot of mean cross-sectional areas for moderate CTS.

provide a more accurate assessment of the extent to which the symptoms may be due to a focal median mononeuropathy versus a generalized peripheral polyneuropathy in such a common situation. The same comment is also applicable for a C6-C7 radiculopathy that may seem clinically similar to CTS. At present time, the issue of which technique should be used because initial screening remains a matter of debate. As an example, Wong et al.[41] and Goldberg et al.[42] proposed diagnostic approaches that involved ultrasonography as the initial screening test for patients suspected with CTS, and secondary electrodiagnostic studies performed only when the ultrasonography results were negative. On the other hand, some authors[43] offered a counterproposal that clinicians should start the screening with nerve conduction study of the median nerve, instead of ultrasonography, because electrodiagnostic study is suggested to be more sensitive for diagnosis of median neuropathy at wrist.[44,45] Despite these debates, there is a broad consensus about the value of ultrasonography in providing complementary information regarding the nerve anatomy and the neighboring structures within the carpal tunnel.

Study Limitations

In the present systematic review, a rigorous literature search was carried out to consolidate the results of all relevant, high-quality studies. However, this study has a number of

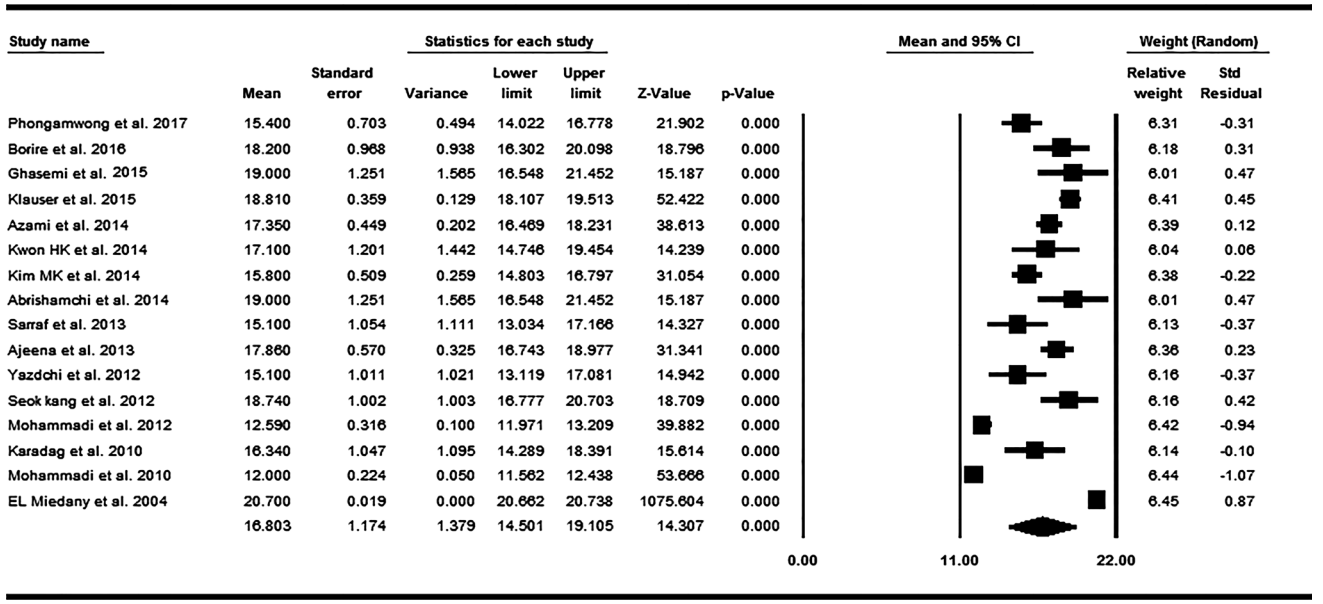

FIGURE 4. The forest plot of mean cross-sectional areas for severe CTS.

TABLE 4. Bias in publications

	Egger's Test			Begg's Test	
Parameters	***t***	**95% CI**	***P***	***Z***	***P***
Mild CTS	0.22	−2.87 to 2.32	0.82	0.99	0.32
Moderate CTS	4.15	−13.93 to −4.44	0.00097	1.71	0.08
Severe	2.95	−14.33 to −2.27	0.01	2.25	0.02

limitations. First, a number of relevant studies were not included in this meta-analysis mainly because their electrodiagnostic criteria for CTS classification were not well described. The second limitation was lack of temperature control in a number of included studies. It is well established that temperature can have a significant effects on neural conduction parameters.[46] Finally, considering the electrodiagnostic studies as the reference method for determination of CTS severity has a limitation because this test may be associated with some false-positive and false-negative results.[47] The possibility of false-positive and false-negative results was neglected in almost all included studies.

CONCLUSIONS

The present meta-analysis synthesized the results of previous studies to provide the overall estimates of median nerve CSA in accordance with the electrodiagnostic classifications of CTS severity. The pooled results showed a median nerve CSA of 11.64 mm^2 for mild, 13.74 mm^2 (adjusted: 13.43 mm^2) for moderate, and 16.80 mm^2 (adjusted: 16.36 mm^2) for severe CTS. These values are of importance for the assessment of patients with CTS using ultrasonography.

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