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The role of diagnostic ultrasound in the examination of carpal tunnel syndrome: an update and systematic review

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ABSTRACT

Background: Diagnostic ultrasound is becoming more available and has potential for identifying carpal tunnel syndrome (CTS), but there is a lack of consensus on optimal measurement parameters and interpretation.

Purpose: The purpose of this systematic review was to analyze and summarize recent published data evaluating measurement properties of diagnostic ultrasound for use in individuals with CTS.

Methods: Five databases were searched to identify studies reporting on diagnostic measurement in individuals $\geq$18 years of age. Thirty-four studies underwent critical appraisal using Center for Evidence Based Medicine guidelines for diagnostic study accuracy. Each team member independently reviewed and scored the studies and consensus was reached through discussion.

Results: Seventeen studies evaluating 21 unique nerve or tunnel measurements and 9 measurement ratios were included. Measurements of median nerve cross sectional area (CSA) taken at the carpal tunnel inlet consistently demonstrated good to excellent interrater reliability (ICC=0.83-0.93) and good intrarater reliability (r>0.81). All studies supported inlet CSA in differentiating between individuals with and without CTS. Carpal tunnel inlet CSA measurements demonstrated a moderate correlation to the Padua severity classification (r = 0.71), but this varied between studies. Diagnostic accuracy of CSA measured at the carpal tunnel inlet using diagnostic cutoff values ranging from 8.5 mm^2 to 12.6 mm^2 resulted in a range sensitivity (63%-96.9%) and specificity (67.9%-100%).

Conclusion: The US measurement most supported was the median nerve CSA measured at the carpal tunnel inlet. There was no evidence supporting the routine use of diagnostic US for individuals with suspected CTS, and no additional evidence to support replacement of electrodiagnostic studies by US. More research is needed to determine use of US for classifying CTS severity or as a differential diagnostic tool for conditions that mimic CTS.

Level of Evidence: N/A

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Introduction

Carpal tunnel syndrome (CTS) is a common compression neuropathy of the median nerve at the wrist level. The lifetime prevalence, regardless of work status, is 7.8%, and it is higher for women than men (10.0% vs 5.8%)[1]. The prevalence also increases linearly with age[1]. Diagnosis of CTS is based on the presence of signs and symptoms found during a clinical exam and may or may not include electrodiagnostic studies, however, there is no single 'gold standard' test or measure for confirming the diagnosis.

Diagnostic ultrasound (US) is frequently reported in the literature as a tool used to examine the morphology of the median nerve. It can provide anatomical or structural information facilitating identification of anatomical variants and concurrent conditions such as ganglion cysts or tenosynovitis[2]. A number of me-

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dian nerve and carpal tunnel ultrasonographic measurements have been used in the assessment of individuals with CTS. A common measure is median nerve cross sectional area (CSA), a measure of nerve swelling[3]. Nerve CSA can be measured at different locations along the forearm and wrist using a direct trace method just inside the hyperechoic rim of the nerve sheath. Ultrasonography can also be used to assess median nerve and carpal tunnel dimensions, median nerve position within the tunnel (palmar displacement), and flexor retinacular (volar) bowing and thickness.

While evidence is conflicting, some authors have found moderate correlations between median nerve CSA measured at the distal wrist crease and subject height[4], weight[5], and wrist circumference[6]. In order to account for body anthropometric variations that could influence nerve CSA, ratios have been used to assess changes in median nerve morphology. Common ratios include: 1) wrist-to-forearm ratio (WFR), which is defined as the ratio between nerve CSA at a distal site, usually the pisiform or distal wrist crease, and CSA of the nerve in the forearm; 2) median-to-ulnar ratio (MUR), or the ratio of median nerve CSA to ulnar nerve CSA, measured at the wrist; and 3) flattening ratio (FR), which is determined by dividing the transverse, radial to ulnar nerve diameter (long axis) by the anterior to posterior nerve diameter (short axis). The FR can be calculated at multiple locations, similar to CSA. Diagnostic US may be beneficial for therapists in the examination of individuals with CTS because it is efficient, less invasive, and less expensive for patients than electrodiagnostic studies, and it is becoming more readily available in rehabilitation settings.

The American Academy of Orthopaedic Surgeons (AAOS) CTS Clinical Practice Guideline published in 2016 reported there was limited evidence against the routine use of US in diagnosing CTS[7]. This Guideline included studies published through February 27, 2015. The authors indicated there were conflicting results when US was compared to electrodiagnostic testing as the reference standard, variability in cutoff values for ruling CTS in and out, and a lack of consensus on the ideal location for obtaining measurements[7]. Guideline authors concluded there was a need for consensus on optimal measurement locations and diagnostic cutoff values in order for US to be considered an effective imaging modality[7]. Since then, a number of studies have provided additional reliability, validity, cutoff, sensitivity, and specificity values of median nerve and carpal tunnel measurements using diagnostic US.

The purpose of this systematic review is to examine and summarize the available data published on the measurement properties of diagnostic US in CTS since February 2015 in order to identify optimal measurement parameters. Specifically, it will describe updated data on reliability, known-group and concurrent validity, cutoff values, sensitivity, specificity, and likelihood ratios.

Methods

Search strategy

PubMed, Embase, the Cumulative Index of Nursing and Allied Health Literature, the Cochrane Library, and Academic Search Complete served as databases to identify studies to include in the review. Searches included articles published between February 27, 2015 to December 31, 2019. The February date was selected as it was the final date of inclusion of articles in the AAOS 2016 Clinical Practice Guideline. Relevant medical subheadings were identified by searching the MeSH database in PubMed and examining prior review articles for search terms. Additional terms were also determined by the research team as articles and ultrasonographic measurements were identified. Search terms included carpal tunnel syndrome, compression neuropathy, carpal tunnel, entrapment neuropathy, median neuropathy, ultrasonography, diagnostic-ultrasound, diagnostic-accuracy, cross-sectional-area, flattening-ratio, swelling-ratio, median-ulnar-ratio, wrist-forearm-ratio, palmar-displacement, sonography, and diagnostic-imaging. Boolean operators were used to connect search terms. The following is an example of a search strategy was used for PubMed:

(carpal tunnel syndrome [MeSH] OR compression neuropathy, carpal tunnel [MeSH] OR entrapment neuropathy, carpal tunnel [MeSH] OR median neuropathy, carpal tunnel [MeSH]) AND diagnostic-ultrasound AND diagnostic-accuracy.

Selection strategy

Primary studies written in the English language that examined the diagnostic accuracy of ultrasonographic median nerve or carpal tunnel measurements in individuals with CTS (ages ≥18) were included in the review. Study designs included cohort, case control, and cross-sectional. Systematic reviews and meta-analyses examining ultrasonographic characteristics in CTS were also included. Studies previously included in systematic reviews and meta-analyses were not included in this review. The following exclusion criteria were applied when reviewing articles: retrospective studies, narrative reviews, case studies, studies with less than 10 participants per group, conference abstracts, studies examining nerve characteristics in healthy participants or participants with diagnoses other than CTS, studies using a contralateral limb as a control, and studies that did not provide enough detail to be replicated.

Data extraction

The following data were extracted from each study: 1) reference information, 2) study design, 3) research question(s), 4) diagnostic properties evaluated, 5) sample size (hands and participants), 6) sample characteristics, 7) methodology, and 8) results including reliability, validity, and diagnostic accuracy.

Critical appraisal

Each researcher completed a critical appraisal of each article using the tool developed by the Center of Evidence Based Medicine for examining accuracy of diagnostic studies. Studies were scored on a scale of 0 to 5[8]. One point was assigned for 1) inclusion of a representative spectrum of participants, 2) all participants receiving the test of interest and the reference test, 3) blinding, 4) appropriate use and presentation of statistics, and 5) repeatability. To examine agreement between raters for the Center of Evidence Based Medicine critical appraisal tool, 5 studies were randomly selected and percent agreement between reviewers was calculated for each item. For item 1, percent agreement between the 3 raters was 87%, for item 2 percent agreement was 73%, and for items 3 through 5, percent agreement was 100%. Studies receiving a score of 2 or less from all reviewers were excluded. Studies receiving a 3 were discussed, and researchers came to consensus on whether or not to include the study. Studies receiving a score of 4 or 5 by all researchers were included in the review (Table 1). The systematic review was scored using the AMSTAR (A Measurement Tool to Assess Systematic Reviews) with a possible total of 11 points (Table 2)[9]. Interrater reliability data for the AMSTAR have previously been reported (Intraclass Correlation Coefficient [ICC] = 0.84)[10]. Score discrepancies were resolved through discussion.

Results

Results of the database searches can be found in the Fig. 1. Overall, out of 34 relevant articles, 16 original studies and one

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Table 1
Article scores following critical appraisal

Study	Score 1[a]	2[b]	3[c]	4[d]	5[e]	Score Total
Atan 2018	0	0	1	1	1	3
Ažman 2018	1	1	0	1	1	4
Chang 2019	0	1	1	1	1	4
Deng 2018	1	1	0	1	1	4
El Habashy 2017	1	1	1	1	1	5
El Shintenaway 2018	1	0	0	1	1	3
Gonzalez-Suarez 2019	0	1	1	1	1	4
Ha 2017	0	1	1	1	1	4
Jiwa 2018	1	0	1	1	1	3
Junck 2015	0	0	1	1	1	3
Köroğlu 2019	0	1	1	1	1	4
Kutlar 2017	1	0	1	1	1	4
Lee 2016	0	1	1	1	1	4
Nkurmah 2018	0	1	1	1	1	4
Phongamwong 2017	1	1	1	1	1	5
Pimental 2018	0	1	1	1	1	4
Roghani (Sensitivity) 2018	0	1	1	1	1	4
Roghani (DX) 2018	0	1	1	1	1	4
Wessel 2019	0	1	1	1	1	4

Key: 1=Yes,0=No or Unclear
[a] Was the test evaluated in a representative spectrum of patients (I.e. all severities)?
[b] All subjects received the test of interest (US) and the reference standard.
[c] Was there an independent, blind comparison between the index test and an appropriate reference ('gold') standard of diagnosis?
[d] Were appropriate statistics presented (sensitivity, specificity, positive predictive values, negative predictive values, likelihood ratios)?
[e] Were the methods for performing the test described in sufficient detail to permit replication?

systematic review were used in the systematic review. Thirteen articles were from PubMed, 2 were from Embase, and 2 were from Academic Search Complete. Ultrasonographic measurements identified in this review included: 1) CSA at the carpal tunnel inlet and outlet, mid-canal, distal radioulnar joint (DRUJ), pronator quadratus, and forearm (various locations); 2) FR measured at the pisiform, hamate, lunate, and mid-canal; 3) carpal tunnel area; 4) median nerve circumference at the inlet, outlet, and mid-canal; 5) longitudinal (radial to ulnar) and transverse (anterior-to-posterior) median nerve diameter taken at the DRUJ, pisiform, scaphoid, and hamate; 6) flexor retinaculum thickness and bowing; 7) MUR with median nerve measures at the carpal tunnel inlet and outlet; 8) median-ulnar difference; 9) inlet CSA to outlet CSA ratio; 10) mean CSA (inlet CSA + outlet CSA/2); 11) WFR with wrist measures taken at the inlet and outlet compared to measures in the forearm; 12) wrist-to-forearm difference with wrist measures taken at the inlet and outlet; and 13) compression ratio (ratio between FR measured at the lunate to FR measured at the pisiform).

Reliability

There were four studies that provided reliability data[11-14]. (Table 3) Intraclass correlation coefficients and r-values were interpreted using values provided by Portney (excellent ≥0.90; good = 0.75-0.89; moderate = 0.50-0.75; and poor ≤ 0.49)[15]. Only one study reported intrarater reliability, and these authors provided data for a sonographer and a radiologist participating in the study[14]. Data were available for CSA of the median nerve at the carpal tunnel inlet, outlet, forearm, and the pronator quadratus; WFR; MUR; inlet-to-outlet (IO) ratio; and FR measured at the hamate. There was variability among studies on the landmark used to identify the carpal tunnel inlet. Authors used the distal wrist crease[11,13], the pisiform[12], or an area between the scaphoid tubercle and the pisiform[14]. Regardless of the landmark used, interrater reliability of the inlet CSA measurement was good to excellent (0.83-0.93) and intrarater reliability was also good for both a radiologist and a sonographer (0.81 and 0.88, respectively)[14]. The most common landmark used to identify the carpal tunnel outlet was the hamate. Interrater reliability of outlet CSA was good (0.84 and 0.86), but there were no intrarater reliability data for outlet CSA identified in this review.

There was variability in the landmarks used to assess median nerve CSA in the forearm. Jiwa et al[11] and Lee and Kim[12] recorded forearm CSA at a site 12 cm proximal to the distal wrist crease, while Junck et al[14] obtained forearm CSA at a midpoint of the measured distance between the distal wrist crease and the antecubital fossa. Interrater reliability values were inconsistent for both forearm CSA (-0.0007[11] and 0.89[14]) and WFR (0.33 to 0.85)[11,12,14], and intrarater reliability values did not exceed 0.69 for these measurements[14].

The interrater reliability of the CSA taken at the pronator quadratus was good (0.85), but intrarater reliability was poor (<0.49)[14]. Interrater reliability of the MUR measured at the distal wrist crease was poor[11]. The IO ratio and FR measured at the hamate demonstrated good interrater reliability (0.81[11] and 0.84-0.86[12], respectively), but there were no intrarater reliability data for IO or FR available in the studies included in this review.

Table 2
Systematic review scores following critical appraisal.

Systematic review	AMSTAR Score 1[a]	2[b]	3[c]	4[d]	5[e]	6[f]	7[g]	8[h]	9[i]	10[j]	11[k]
Torres-Costoso 2018	1	1	0	0	0	1	1	1	1	1	1

Key: 1=criteria is present, 0= criteria not present.
[a] Was an 'a priori' design provided?
[b] Was there duplicate study selection and data extraction?
[c] Was a comprehensive literature search performed?
[d] Was the status of publication (i.e. grey literature) used as an inclusion criterion?
[e] Was the list of included and excluded studies provided?
[f] the characteristics of the included studies provided?
[g] Was the scientific quality of the included studies assessed and documented?
[h] the scientific quality of the included studies used appropriately in formulating conclusions?
[i] the methods used to combine study findings appropriate?
[j] the likelihood of publication bias assessed?
[k] Was the conflict of interest stated?

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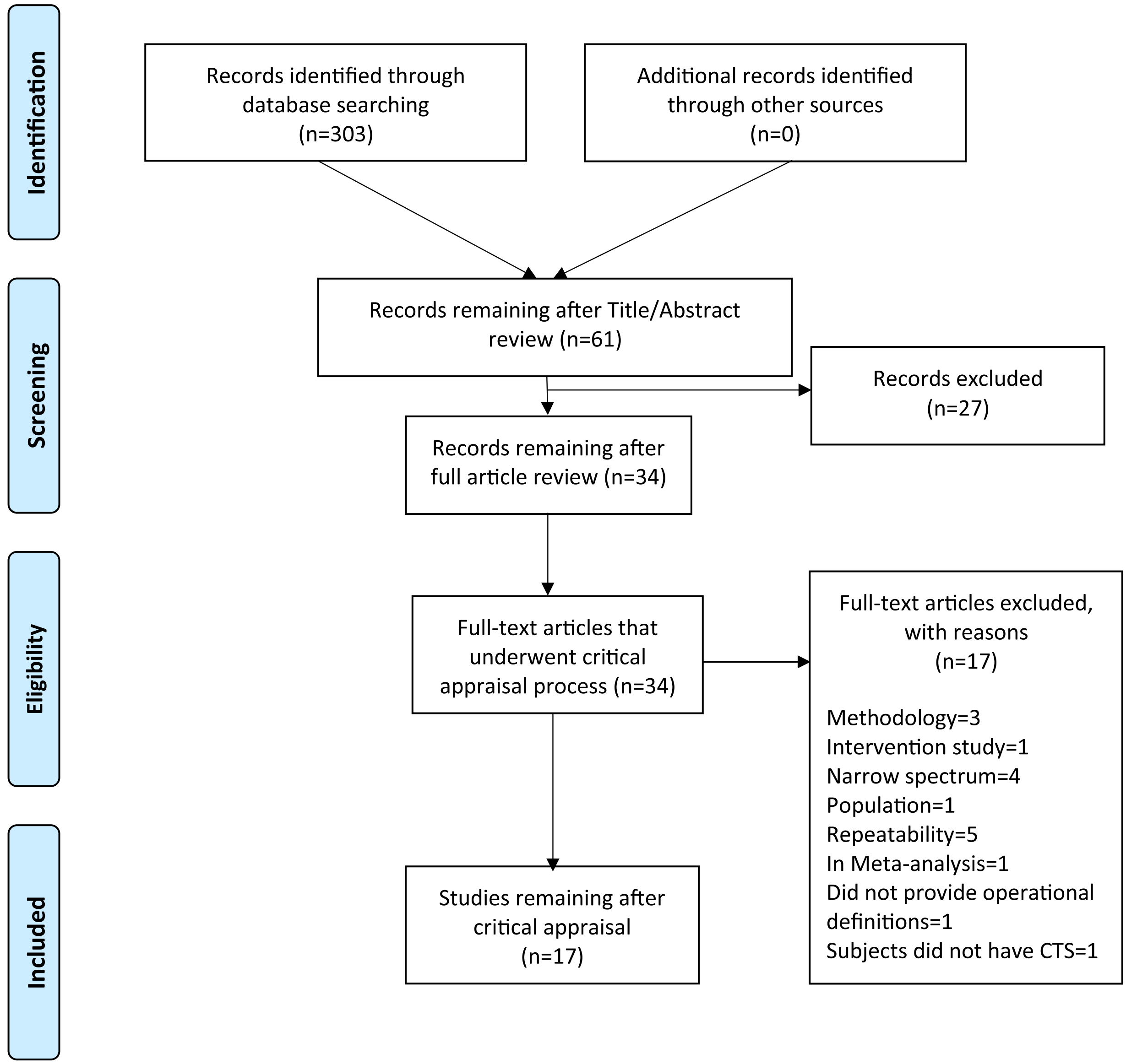

Fig. 1. Search results.

Table 3
Reliability values of sonographic measurements identified in this review.

Measurement	Study	Inter-rater reliability	Intra-rater reliability
Median nerve CSA (inlet)	Jiwa et al	ICC=0.93 ($CI_{95\%}$ 0.75, 0.98)	
	Phongamwong et al	ICC=0.93 ($CI_{95\%}$ 0.87, 0.96)	
	Junck et al	r=0.93 (P<0.0001)	Sonographer r=0.88; Radiologist r=0.81
	Lee and Kim	Using cut-off value >8.5 mm^2 ICC=0.85	
		Using cut-off value >9.0 mm^2 ICC=0.85	
		Using cut-off value >10.7 mm^2 ICC=0.87	
		Using cut-off value >15.0 mm^2ICC=0.83	
Median nerve CSA (outlet)	Jiwa et al	ICC=0.86 ($CI_{95\%}$ 0.53, 0.96)	
	Lee and Kim	Using cut-off value >12.0 mm^2 ICC=0.84	
Median nerve CSA (forearm)	Jiwa et al	ICC=0.0007 ($CI_{95\%}$ -0.60, 0.60)	
	Junck et al	r=0.89 (P<0.0001)	Sonographer r=0.67; Radiologist r=0.55
Median nerve CSA (PQ)	Junck et al	r=0.85 (P<0.0001)	Sonographer r=0.15; Radiologist r=0.49
Wrist-to-forearm ratio	Jiwa et al	ICC=0.33 ($CI_{95\%}$ -0.34, 0.78)	
	Lee and Kim	Using cut-off value ≥1.4 ICC=0.85	
	Junck et al	r=0.73 (P<0.0001)	Sonographer r=0.69; Radiologist r=0.44
Median-to-ulnar ratio	Jiwa et al	ICC=0.25 ($CI_{95\%}$ -0.41, 0.74)	
Inlet-to-outlet ratio	Jiwa et al	ICC=0.81 ($CI_{95\%}$ 0.40, 0.95)	
Flattening ratio (hamate)	Lee and Kim	Using cut-off value ≥4.2 ICC=0.86	
		Using cut-off value ≥3.4 ICC=0.84	

CI, confidence interval; CSA, cross-sectional area; ICC, intraclass correlation coefficient; PQ, pronator quadratus

Table 4
Known-group validity of sonographic measurements identified in this review.

Measurement	Study (measurement units)		CTS mean (SD)	Control mean (SD)	Mean Difference	P-value
Median nerve CSA (inlet)	Atan et al (mm^2)		14.51 (3.72)	9.33 (2.07)	5.17	<0.001
	Ažman et al (mm^2)		15.3 (5.15)	8.2 (1.43)	7.1	<0.001
	El Habashy et al (mm^2)		16.47 (4.28)	8.05 (1.49)	8.42	<0.0001
	Jiwa et al (mm^2)		14.96 (5.13)	8.37 (2.28)	6.59	<0.001
	Kutlar et al (cm^2)		0.13	0.08	0.05	<.0000
	Gonzalez-Suarez et al (cm^2)		0.08 (0.02)	0.07 (0.02)	0.01	0.02
	Köroğlu et al (cm^2)		*	*	*	<0.001
	Chang et al (mm^2)		11.3 (4.4)	8.8 (2.2)	2.5	<0.0001
Median nerve CSA (outlet)	Ažman et al (mm^2)		15.4 (5.37)	8.8 (1.74)	6.6	<0.001
	Jiwa et al (mm^2)		10.09 (3.28)	7.44 (2.09)	2.65	<0.001
	Gonzalez-Suarez et al(cm^2)		0.10 (0.03)	0.08 (0.02)	0.02	<0.01
	Köroğlu et al (cm^2)		*	*	*	<0.001
Median nerve CSA (mid-canal)	Ažman et al (mm^2)		11.6 (4.12)	8.2 (1.85)	3.4	<0.001
Median nerve CSA (DRUJ)	Chang et al (mm^2)		8.2 (2.9)	7.4 (1.7)	0.8	0.04
	Köroğlu et al (cm^2)		*	*	*	<0.001
Median Nerve CSA (PQ)	Junck et al (mm^2)	sonographer	10.6 (1.7)	9.5 (1.8)	1.1	0.68
		radiologist	11.5 (1.9)	9.8 (1.3)	1.7	0.003
Mean CSA (CSA inlet+CSA outlet/2)	Ažman et al (mm^2)		15.3 (4.04)	8.5 (1.33)	6.8	<0.001
Flattening ratio (pisiform)	Köroğlu et al		*	*	*	0.001
	Chang et al		2.5 (0.7)	2.6 (0.9)	0.1	0.64
	Lee and Kim	right	3.0 (0.8)	2.8 (0.4)	0.2	0.167
		left	3.0 (0.7)	2.7 (0.4)	0.3	0.372
Flattening ratio (hamate)	Köroğlu et al		*	*	*	0.679
	Lee and Kim	right	3.2 (0.4)	2.8 (0.4)	0.4	<0.001
		left	3.1 (0.4)	2.7 (0.4)	0.4	0.004
Flattening ratio (mid-canal)	Ažman et al		4.1 (1.63)	3.7 (1.17)	0.4	0.191
Flattening ratio (lunate)	Lee and Kim	right	2.7 (0.5)	2.7 (0.4)	0	0.609
		left	2.9 (0.5)	2.6 (0.4)	0.3	0.173
Median-to-ulnar ratio	Atan et al		3.75 (0.86)	2.72 (0.75)	1.03	<0.001
	Jiwa et al		3.10 (1.19)	1.75 (0.39)	1.35	<0.001
	Chang et al		4.1 (2.3)	2.9 (1.5)	1.2	0.0206
Inlet-to-outlet ratio	Ažman et al		1.1 (0.51)	1.0 (0.21)	0.1	0.235
	Jiwa et al		1.53 (0.61)	1.13 (0.17)	0.40	0.001
	Gonzalez-Suarez et al		0.87 (0.19)	0.93 (0.22)	-0.06	0.06
Swelling ratio	Köroğlu et al		*	*	*	<0.001
	Chang et al		1.5 (0.9)	1.2 (0.3)	0.3	0.04
Wrist-to-forearm ratio	Ažman et al		2.4 (0.79)	1.5 (.27)	0.9	<0.001
	El Habashy et al		3.07 (0.89)	1.26 (0.26)	1.81	<0.0001
	Jiwa et al		2.44 (0.77)	1.28 (0.39)	1.16	<0.001
	Gonzalez-Suarez et al		1.71 (0.63)	1.69 (0.71)	0.02	0.82
	Lee and Kim	right	1.9 (0.5)	1.1 (0.2)	0.8	<0.001
		left	1.9 (0.5)	1.1 (0.2)	0.8	<0.001
Outlet-to-forearm ratio	Ažman et al		2.4 (0.82)	1.5 (0.31)	0.9	<0.001
	Gonzalez-Suarez et al		2.01 (0.67)	1.88 (0.83)	0.13	0.32
Flexor retinacular bowing	Ažman et al (mm)		4.5 +/- 0.82	3.9 +/- 0.45	0.6	<0.001
	Köroğlu et al (mm)		*	*	*	<0.001
	Gonzalez-Suarez et al (cm)		0.21 +/- 0.11	0.21 +/- 0.19	0	0.83
Flexor retinacular thickness	Köroğlu et al	DRUJ	*	*	*	0.171
		pisiform	*	*	*	0.057
Median nerve circumference	Ažman et al (mm)	inlet	17.9 +/- 3.05	13.6 +/- 1.55	4.3	<0.001
		outlet	19.8 +/- 3.43	15.9 +/- 2.09	3.9	<0.001
		mid-canal	17.3 +/- 3.48	14.5 +/- 3.4	2.8	<0.001
Carpal tunnel area	Köroğlu et al		*	*	*	0.516
Median nerve diameter	Köroğlu et al		*	*	*	<0.001
Wrist (inlet)-to-forearm difference	Gonzalez-Suarez et al (cm)		0.03 +/- 0.03	0.02 +/- 0.06	0.01	0.16
Wrist (outlet)-to-forearm difference	Gonzalez-Suarez et al (cm)		0.03 +/- 0.06	0.05 +/- 0.03	0.02	0.01
Median-to-ulnar difference	Chang et al (mm2)		8.2 +/- 4.3	5.3 +/- 2.0	2.9	<0.0001
Compression ratio	Lee and Kim	right	1.2 +/- 0.6	1.0 +/- 0.3	0.2	0.263
		left	1.1 +/- 0.2	1.1 +/- 0.3	0	0.620

CSA, cross-sectional area; DRUJ, distal radio-ulnar joint; PQ, pronator quadratus; SD, standard deviation.
* data not reported.

Known-group validity

Data were available from 10 studies on known-group validity comparing measures from individuals with CTS to a control group (Table 4)[11,12,14,16-22]. In all studies reporting on median nerve CSA measurements taken at the DRUJ, within the canal, and at the carpal tunnel inlet and outlet showed a higher CSA in the CTS group compared to the control group ($P < .04$). The largest difference between those with and without CTS was reported by El Habashy et al[18] for the CSA measured at the carpal tunnel inlet. In their study, the CTS group had a mean CSA of 16.47 mm^2 versus the control group 8.05 mm^2 (mean difference [MD] = 8.42 mm^2). Mean CSA, MUR, swelling ratio, median nerve circumference and diameter, wrist-to-forearm CSA difference (wrist measurement taken at the outlet), and median-to-ulnar difference all showed statistically significant differences between those with and without CTS ($P < .04$). Flexor retinacular thickness, FR measured mid-canal and at the lunate, carpal tunnel area, compression ratio,

Table 5
Correlation between ultrasonographic measurements and nerve conduction parameters identified in this review.

Measurement	Study	DML (r, p-value)	DSL (r, p-value)	Motor amplitude (r, p-value)	Sensory amplitude (r, p-value)	Sensory conduction velocity (r, p-value)	Palmar-median interlatency (r, p-value)
Median nerve CSA (inlet)	El Habashy et al	0.62 (0.0001)	0.60 (0.0001)	-0.56 (0.0001)	-0.55 (0.0001)		
	El Shintenaway et al	0.58 (<0.001)	0.46 (<0.001)		-0.30 (0.027)	-0.56 (<0.001)	
Flattening ratio (pisiform)	El Shintenaway et al	0.19 (0.16)	0.29 (0.029)		-0.16 (0.24)	-0.05 (0.71)	
Flattening ratio (hamate)	El Shintenaway et al	0.24 (0.12)	-0.01 (0.95)		-0.19 (0.39)	-0.59 (0.003)	
Median-to-ulnar ratio	Jiwa et al	0.34 (0.03)					0.35 (0.04)

CSA, cross-sectional area; DML, distal motor latency; DSL, distal sensory latency.

Table 6
Correlations between severity and surgical outcome compared to ultrasonographic findings.

Measurement	Study	Severity using Padua Classification (r-value, p-value)	Severity using Bland Classification (r-value, p-value)
Median nerve CSA (inlet)	Ažman et al	0.71 (<0.001)	
	Ha et al		0.32 (0.02)
Median nerve CSA (outlet)	Ažman et al	0.61 (<0.001)	
	Ha et al		0.23 (0.09)
Median nerve CSA (mid-canal)	Ažman et al	0.45 (<0.001)	
Mean CSA (Inlet CSA + Outlet CSA/2)	Ažman et al	0.74 (<0.001)	
Flattening ratio (mid-canal)	Ažman et al	0.15 (0.021)	
Inlet-to-outlet ratio	Ažman et al	0.11 (0.10)	
Wrist-to-forearm ratio	Ažman et al	0.59 (<0.001)	
Outlet-to-forearm ratio	Ažman et al	0.47 (<0.001)	
Flexor retinacular bowing	Ažman et al	0.32 (<0.001)	
Median nerve circumference (inlet)	Ažman et al	0.66 (<0.001)	
Median nerve circumference (mid-canal)	Ažman et al	0.45 (<0.001)	
Median nerve circumference (outlet)	Ažman et al	0.53 (<0.001)	
Flexor retinacular bowing	Ažman et al	0.32 (<0.001)	

CSA, cross-sectional area; PQ, pronator quadratus; WFR, wrist-to-forearm ratio

and wrist-to-forearm difference (wrist measurement taken at the inlet) showed no significant difference between individuals with and without CTS ($P > .05$). There was conflicting evidence on all other measures (Table 4).

Concurrent validity

There were six studies that examined concurrent validity of ultrasonographic measures using a variety of reference standards including nerve conduction parameters (Table 5)[11,18,23], CTS severity grades using scales based on results of nerve conduction studies (Table 6)[17,24], and results of the Carpal Tunnel Questionnaire-Symptom Severity Scale[25]. There were no correlation coefficients between ultrasonographic measurements and reference standards that exceeded 0.74. Ažman et al[17] found the highest correlation coefficients between median nerve CSA measured at the carpal tunnel inlet and mean CSA and CTS severity using the Padua Classification (r = 0.71; $P < .001$ and r = 0.74; $P < .001$, respectively).

Wessel et al[25] examined the relationship between median nerve CSA measured at the pronator quadratus, pisiform, and hamate and scores on the Levine-Katz Symptom Severity Scale. There were no significant correlation coefficients between individual CSA measurements and Symptom Severity Scores (r <0.14; $P > .41$) These authors also examined the relationship between CSA change scores (Δ CSA: pisiform to hamate, pronator quadratus to pisiform, and pronator quadratus to hamate) and scores on the Levine Katz Symptom Severity Scale. They reported two significant correlation coefficients, but the magnitude of each was low (Δ CSA pisiform to hamate r = 0.36; $P < .05$; Δ CSA pronator quadratus to hamate r = 0.37; $P < .05$)[25].

Authors of two studies examined agreement between the presence of US findings, surgical resolution of symptoms[26], and the presence of electrodiagnostically confirmed CTS[12]. According to Pimentel et al[26], of the individuals who presented with a median nerve inlet CSA greater than 10 mm^2 prior to carpal tunnel release, 76.5% had surgical resolution of symptoms. The kappa coefficient, or level of agreement between finding a CSA >10 mm^2 (Yes/No) and having resolution of symptoms following surgery (Yes/No) was 0.42 ($P < .001$) suggesting moderate agreement. In the same study, authors reported that in individuals who had CTS confirmed through nerve conduction studies, 83.5% reported surgical resolution of symptoms (κ = 0.65; $P < .001$) Agreement between positive US findings (inlet CSA >10 mm^2) and positive nerve conduction studies was 0.232 ($P = .006$)[26].

Using cutoff values for diagnostic US extracted from the literature, Lee and Kim[12] examined the agreement between the presence of various US findings and the presence of electrodiagnostically-confirmed CTS. Authors reported fair agreement with presence of CTS and FR measured at the hamate (cutoff value ≥4.2; $\kappa = 0.38$) and moderate agreement with outlet CSA (cutoff value >12.0 mm^2; $\kappa = 0.55$), inlet CSA (cutoff >10.7 mm^2; $\kappa = 0.51$ and cutoff value >9.0 mm^2; $\kappa = 0.60$), and FR measured at the hamate (cutoff value ≥3.4; $\kappa = 0.42$). Authors found substantial agreement between electrodiagnostically-confirmed CTS and inlet CSA (cutoff value >8.5; $\kappa = 0.64$). In addition, when using a cutoff value of 1.4 for WFR, there was substantial agreement with electrodiagnostically-confirmed CTS ($\kappa = 0.71$). In this study, WFR was calculated using CSA measurements taken from the distal wrist crease and the forearm 12 cm proximal to the distal wrist crease.

Diagnostic accuracy

Several studies ($n = 11$) included in this review examined cutoff values for the optimal diagnostic accuracy of ultrasonographic measures (Table 7A and B)[11,13,28,16,17,19,21-23,26,27]. Mea-

Table 7A
Diagnostic accuracy for median nerve cross-sectional area measures at the carpal tunnel inlet and outlet.

Study	Diagnostic Accuracy of the Median Nerve CSA at the Carpal Tunnel Inlet					Diagnostic Accuracy of the Median Nerve CSA at the Carpal Tunnel Outlet				
	Cut-off value (mm^2)	Sn (%)	Sp (%)	PLR[a]	NLR	Cut-off value (mm^2)	Sn (%)	Sp (%)	PLR	NLR
Atan et al	>11.95	80.0	80.0	4.0	0.25	-	-	-	-	-
Ažman et al (overall)	>10	87.4	94.6	16.2	0.13	11	74.1	92.5	9.9	0.28
Ažman et al (clinically mild cases, n=83)	>10	94.2	89.2	8.8	0.06	-	-	-	-	-
Chang et al	>10.35	63	84	3.9	0.44	-	-	-	-	-
El-Shintenawy et al	> 9*	80.4	100.0	Infinity (or >804)	0.20	-	-	-	-	-
Jiwa et al	>10.22	93.0	89.0	8.6	0.08	-	-	-	-	-
Köroğlu et al	>12.5	88	96	22	0.13	8.5	52	85	3.47	0.56
Kutlar et al	>10	90.9	94.0	15.0	0.11	-	-	-	-	-
Phongamwong et al	>11.5	69.2	67.9	2.1	0.46	-	-	-	-	-
Pimentel et al	>10	84.6	81.8	4.7	0.19	-	-	-	-	-
Roghani et al	>8.5	96.9	93.6	15.1	0.03	11.5	72.2	53.2	1.5	0.53
Torres-Costoso et al (pooled data from systematic review)	ranged from 9-12.6	81	84	6.22	0.16	ranged from 9-10	74	76	4.63	0.25

CSA, cross-sectional area; NLR, negative likelihood ratio; PLR, positive likelihood ratio; Sn, sensitivity; Sp, specificity
cutoff values converted to mm^2 from cm^2 as appropriate.
[a] PLR/NLR calculated from sensitivity and specificity values:Calculations used: PLR = sensitivity/(1-specificity) and NLR = (1-sensitivity)/(specificity)

Table 7B
Diagnostic accuracy for median nerve cross-sectional area inlet-to-outlet ratio and flattening ratio measured at the hamate.

Study	Diagnostic Accuracy of the Median Nerve CSA Inlet-to-Outlet Ratio					Diagnostic Accuracy of the Median Nerve Flattening Ratio (measured at the hamate)				
	Cut-off value (mm^2)	Sn (%)	Sp (%)	PLR[a]	NLR	Cut-off value (mm^2)	Sn (%)	Sp (%)	PLR	NLR
El-Shintenawy et al	-	-	-	-	-	>4	91.3	100.0	Infinity	0.09
Jiwa et al	>1.27	56.0	84.0	3.5	0.52	-	-	-	-	-
Köroğlu et al	-	-	-	-	-	>3.54	28.9	92.5	3.85	0.77

CSA, cross-sectional area; NLR, negative likelihood ratio; PLR, positive likelihood ratio; Sn, sensitivity; Sp, specificity
cutoff values converted to mm^2 from cm^2 as appropriate.
[a] PLR/NLR calculated from sensitivity and specificity values:Calculations used: PLR = sensitivity/(1-specificity) and NLR = (1-sensitivity)/(specificity).

sures greater than the cutoff value indicate the presence of CTS (a positive test) and measures less than the cutoff value indicate a normal finding. Electrophysiological studies were used consistently as the reference standard to confirm or rule out the diagnosis. Sensitivity, specificity, as well as positive and negative likelihood values associated with the given cutoff value were the most commonly reported statistics. Where likelihood ratios were not given, values were calculated by the researchers. Given the numerous measures examined in these articles, diagnostic accuracy will be reported on the ultrasonographic measures that demonstrated consistent, acceptable reliability and known-group validity.

Mean cutoff values for CSA of the median nerve at the carpal tunnel inlet ranged from 8.5 mm^2 to 12.6 mm^2 (Table 7A). Sensitivity values ranged from 63% to 96.9%, while specificity values ranged from 67.9%-100%. Positive likelihood ratio values ranged from 2.1 to infinity, indicating anywhere from a small but sometimes important shift to large and conclusive shifts in pre- to post-test probability of being diagnosed with CTS given a positive test (CSA measuring at or greater than the CSA cutoff range)[29]. Negative likelihood ratio values range from 0.46-0.03 indicating small but sometimes important shifts to large and conclusive shifts of not having CTS given a negative test (CSA measuring smaller than the stated cutoff range)[29].

Four studies examined the mean cutoff values for CSA of the median nerve at the carpal tunnel outlet which ranged from 8.5-11.5 mm^2 (Table 7A)[17,21,27,28]. Sensitivity values ranged from 52%-74.1% and specificity values ranged from 53.2%-92.5%. Positive likelihood ratio values ranged from 1.5 to 9.9, indicating a range from negligible shifts to large and conclusive shifts in pre- to post-test probability of being diagnosed with CTS given a positive test. Negative likelihood ratio values range from 0.56-0.25 indicating negligible shifts to small shifts of not having CTS given a negative test[29]. Only one study reported on the accuracy of the median nerve CSA inlet to outlet ratio[11] and two studies reported the diagnostic accuracy of the flattening ratio (measured at the hamate) (Table 7B)[21,23].

Discussion

The purpose of this review was to report on measurement properties of diagnostic ultrasound in CTS published since the 2016 AAOS Clinical Practice Guideline and to determine if there is new evidence that would help in establishing recommendations for use in the clinical setting. Since publication of the AAOS Guideline, several good to high quality studies have provided additional properties on ultrasonographic measures. Only measures showing good to excellent interrater and/or intrarater reliability data identified in this review will be discussed in detail. These measures include CSA measured at the carpal tunnel inlet and outlet, the inlet-to-outlet ratio, and flattening ratio.

Inlet cross sectional area

Reliability and known-group validity of CSA measurements taken at the carpal tunnel inlet are consistently well-supported in the literature. All studies reported good to excellent inter- and intrarater reliability using the direct trace method. These findings are consistent with prior studies examining inter- and intrarater reliability of inlet CSA[30-34]. Current findings are also consistent with interrater reliability values found in the asymptomatic population (ICC = 0.94)[5]. All studies examining known-group validity of inlet CSA support its use in differentiating between those with and without CTS[11,16-22].

Studies examined in this review reported statistically significant correlation coefficients between inlet CSA and electrodiagnostic test results; however, the highest correlation coefficient between inlet CSA and severity using the Padua scale was 0.71[17]. A limitation of this study was that it lacked researcher blinding. In a study from 2012, Kim et al[35] found a weak correlation (r = 0.43) between inlet CSA and severity using the Padua classification. Ha et al[24] used the Bland classification as the reference standard and found the correlation between inlet CSA and severity was 0.32. One reason for this difference may be that Ha et al[24] collapsed the 7-point Bland classification into an arbitrary 4-point scale. In this classification, Bland electrophysiological severity grades 1 and 2 were labeled Grade I, Bland grades 3 and 4 were regrouped into Grade II, and Bland severity grades 5 and 6 were reclassified into Grade III. Individuals with normal electrophysiological findings were labeled Grade 0.

In other studies reporting on correlations between inlet CSA and sensory conduction velocity and distal motor latency, both of which are parameters used in the Padua and Bland severity scales, the magnitude of the coefficients were lower than that reported by Azman et al[17] (-0.56[23] and -0.62[18]). Correlations between inlet CSA and sensory amplitude and distal sensory latency varied. One study included in this review reported a correlation coefficient of -0.30 between inlet CSA and sensory amplitude[23], while El Habashy et al[18] reported a moderate correlation (r = -0.55). These differences may be due to different testing protocols and interpretation of results used in different labs. In addition, the two tests, US and nerve conduction studies, are measuring different constructs. Ultrasound assesses nerve morphology while nerve conduction studies provide information on nerve function. Also, the US examiner in the Azman study was not blinded to electrodiagnostic or clinical findings.

The findings of this systematic review indicate a 3.1%-37% false negative rate and a 0-32.1% false positive rate when diagnosing CTS, using inlet CSA cutoff values between 8.5 mm^2 to 12.6 mm^2. Therefore, this test appears to be slightly better at correctly identifying CTS when the inlet CSA is at or greater than the cutoff range than it is in ruling out CTS when the test is negative. This is due to a slightly higher false negative rate. These results are consistent with the meta-analysis conducted by Torres et al[28]. Roghani et al[27] and El-Shintenawy et al[23] also reported excellent diagnostic accuracy of inlet CSA in which cutoff values were 8.5 mm^2 and 9 mm^2, respectively. Therefore, a larger cutoff value did not consistently result in greater diagnostic accuracy.

Pimentel et al[26] examined the diagnostic accuracy of both ultrasonographic measures and nerve conduction studies in females using remission of paresthesias (determined by change in Carpal Tunnel Questionnaire-Symptom Severity Scale) 4 months after surgery as the reference standard. Ultrasonographic evaluation of inlet CSA using a cutoff value of 10 mm^2 and results of standardized nerve conduction studies (sensory nerve conduction velocity and distal motor latency) demonstrated no statistically significant difference in sensitivity [US = 84.6% (95%CI: 76.2, 90.9); NCV = 92.3% (95%CI: 85.4, 96.6)], specificity [US = 81.8 (95% CI: 48.2, 97.7); NCV = 90.9 (95% CI: 58.7, 99.8)], positive likelihood ratio [US = 4.7 (95% CI: 1.3, 16.4); NCV = 10.2 (95% CI: 1.6, 65.9)], or negative likelihood ratio [US = 0.2 (95% CI: 0.1, 1.3) NCV = 0.1 (95% CI 0–0.2)]. The results of this study indicate false positive rates of 18.2% for inlet CSA using a cutoff of 10 mm^2 and 9.1% for NCV. The false negative rates of US and NCV are 15.4% and 7.7%, respectively.

Although, both diagnostic measures appear to effectively detect CTS, results of nerve conduction studies showed better agreement with postoperative resolution of symptoms at 4 months than inlet CSA. One might also expect inlet CSA to be highly correlated with CTS symptom severity. Wessel et al[25] found statistically significant correlations between symptom severity and changes in nerve CSA along the forearm and wrist; however, the magnitude of these correlations was low (r<0.42). This suggests that factors in addition to CSA or nerve morphology influence symptoms.

It does appear that the severity of CTS influences the diagnostic accuracy of median nerve CSA. Azman et al[17] demonstrated that in cases of mild CTS, when inlet median nerve CSA is larger than 10 mm^2, more false positives (10.8%) were noted when compared to the group of people with CTS as a whole. In mild CTS, when the inlet CSA was less than 10 mm^2, there were fewer false negatives (5.4% false negative rate). Therefore, the sensitivity of this cutoff value is better and the specificity is slightly worse in cases of mild CTS when compared to cases that are more severe.

Outlet cross sectional area

Studies included in this review showed good interrater reliability of measurements of median nerve CSA taken at the carpal tunnel outlet. However, prior reliability studies are conflicting, with reliability values ranging from 0.39 to 0.88.[32,34] All studies included in this review support the use of outlet CSA measurements to differentiate between those with and without CTS, but the studies examining correlations with severity scales based on electrodiagnostic classifications are conflicting. In comparing data on inlet and outlet CSA, there is more evidence to support the use of measuring CSA at the carpal tunnel inlet. The diagnostic accuracy values including sensitivity, specificity, and positive and negative likelihood ratios were consistently less for outlet CSA when compared to inlet CSA. This conclusion is similar to findings from two prior systematic reviews[28,36]. Torres et al[28] reported the diagnostic accuracy of inlet CSA measurements was higher than that for the outlet, and inlet CSA was more reliable.

Inlet-to-outlet ratio

The CSA IO ratio measured at the hamate showed good reliability, but this measure demonstrated conflicting evidence when comparing measurements between those with and without CTS. Azman et al[17] and Gonzalez-Suarezet al[20] reported no significant difference when comparing IO ratios in those with and without CTS, and Jiwa et al[11] reported a larger IO ratio in those with CTS, but the MD between groups was small (MD = 0.40; P = .001). There was no correlation between IO ratio and severity using the Padua classification (r = 0.11)[17]. Only one study examined the diagnostic accuracy of the IO ratio, and this measure demonstrated less diagnostic accuracy than measures of inlet CSA when using IO ratio of 1.27 as a cutoff value[11].

Flattening ratio

Median nerve FR is a measure of nerve compression. Flattening ratio measured at the hamate showed good interrater reliability in one study included in this review, but prior studies have shown conflicting results[33,34]. Ooi et al[33] reported interrater reliability values between 0.44 and 0.58, and Wang et al[34] reported the 95% confidence interval for interrater reliability ranged from 0.58

and 0.84. There was conflicting evidence on the ability of FR measured at the hamate to differentiate between those with and without CTS. Köroğlu et al[21] reported no significant difference (MD not reported; $P = .68$) while Lee and Kim[12] reported statistically significant differences when examining both right and left hands between those with and without CTS (MD 0.40; $P < .004$). The same is true for FR when measured at the pisiform level. Studies identified in this review and prior literature show there is conflicting evidence on known-group validity of FR assessed at the pisiform level[12,21,22,37,38]. Köroğlu et al[21] and Azami et al[38] reported statistically significant differences between groups. Mean values were not reported by Köroğlu et al[21], but Azami et al[38] reported the mean FR for those with CTS was 1.83 and those without was 0.88 ($P = .001$) when measured at the pisiform. Chang et al[22], Lee and Kim[12], and Roll et al[37] reported no differences between FR (pisiform) in those with CTS and those without (MDs <0.30; $P > .17$).

Median nerve compression is a primary factor in the pathogenesis of CTS, and it seems plausible that FR would be an objective measure of compression. Buchberger et al[39] reported a significantly higher FR measured at the distal tunnel, or hamate, when compared to the FR measured at the pisiform or distal radius. These authors also reported an increase in CSA at the inlet suggesting compression at the distal tunnel resulted in swelling at the proximal tunnel[39]. Findings in this review concur with evidence of a swollen median nerve captured by measuring inlet CSA, but measures of the FR were less consistent. If the measure is not taken at the site of compression, flattening may not be captured in the US assessment. Chronic nerve compression leads to a breakdown in endoneurial blood flow which results in neural edema and eventually fibroblast production and nerve scarring[40]. This is more consistent with the enlarged CSA rather than FR. The two studies that examined the diagnostic accuracy of the FR both demonstrated excellent specificity with a false positive rate of 0-7.5%; however, the false negative rate was much more variable (8.7%-71.1%)[21,23].

Some measurement properties of WFR are promising. Azman et al[17] found a moderate correlation between WFR and CTS severity, and Lee and Kim[12] showed substantial agreement between WFR >1.4 and presence of CTS as determined by electrodiagnostic testing. However, the results of this review identified issues with reliability of this measurement. This is likely due to the variability in the location from which the forearm measurement was taken and perhaps methodological difficulty in obtaining the forearm CSA measurement. The most common site used in the identified studies in this review (12 cm proximal to the wrist crease) showed the highest variability in interrater reliability (0.33-0.85). A prior study by Mhoon et al[31], who also measured forearm CSA 12 cm proximal to the distal wrist crease, showed interrater reliability equal to 0.96. While some measurement properties of WFR are acceptable, reliability and standardization of the landmarks used should be improved.

Some studies have suggested that US can be used in place of electrodiagnostic testing. Based on findings from this review, there is not enough evidence to show the two testing modalities can be used interchangeably. First, the two examinations are measuring different constructs, anatomy and function, and the magnitude of the correlations identified in the studies are moderate at best and are conflicting across some studies and measurements. Other authors have suggested using US and electrodiagnostics to complement one another[2,36]. Goldberg et al[2] suggested using US as a screening tool, but if the patient showed evidence of possible cervical radiculopathy, peripheral neuropathy, or brachial plexopathy, then the patient should proceed directly to electrodiagnostic testing for differential diagnosis. Also, some US measurements may be useful in differentiating between those with and without CTS, but there are no data on the ability of US to discriminate between CTS and pathologies that have signs and symptoms that mimic CTS.

This review was limited to data reported from 2015 to present. This was done to show new evidence that has emerged since publication of the AAOS CTS Clinical Practice Guideline. Measures that did not have recent, high-quality published data were not included in this review. For example, palmar displacement of the median nerve within the tunnel appeared in one study[11], but the authors did not provide an accurate description of how this measure was obtained, and therefore data for this measurement were not included in this review. Also, some measures with good known-group validity identified in this review were not reported on in depth because the authors were unable to identify high-quality reliability data on individuals with CTS, either from studies included in this review or in studies published prior to February 2015. For example, mean CSA (inlet CSA+outlet CSA/2), median nerve diameter, and median-to-ulnar difference may have promise, but more research is needed to establish reliability in individuals with CTS. Another limitation is that only studies in the English language were included. Additionally, it should be noted that assessor experience, equipment used, measurement parameters, and differences in reference standards were highly variable among included studies limiting the ability to identify a measurement parameter with a consistently strong body of evidence to support its use in practice. Finally, administration of EMG testing and classification patients according to electrodiagnostic findings with CTS could have affected criterion validity and thus the diagnostic accuracy values obtained among the studies.

Conclusion

Additional measurement properties studied since the AAOS Clinical Practice Guideline have been reported. Based on results of this study, the sonographic measurement most supported by evidence is median nerve CSA measured at the carpal tunnel inlet. There is no evidence to support this measure or the use of US in general as a replacement for electrodiagnostic studies. There is no additional evidence to support the use of diagnostic US on a routine basis for individuals with suspected CTS, and more research is needed to determine the ability of diagnostic US to differentiate between CTS of different severities and conditions that mimic CTS. Diagnostic US may provide additional information regarding anatomic variation and the presence of additional structures contributing to median nerve impairment. This knowledge could facilitate clinical decisions for non-surgical management by hand therapists or referral to a surgeon.

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