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DIAGNOSTIC TEST ACCURACY OF TINEL'S TEST IN ADULTS WITH CARPAL TUNNEL SYNDROME – A SYSTEMATIC REVIEW.

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Abstract:	Background Tinel's test is commonly used in the diagnosis of carpal tunnel syndrome (CTS) despite its questionable diagnostic test accuracy (DTA). This systematic review investigated the DTA of Tinel's test in CTS using electrodiagnosis as the reference standard and explored the heterogeneity between included studies. Methods Prospective studies evaluating Tinel's test in adults with CTS were included. The principal measures were sensitivity and specificity. A literature search was conducted for studies published up to 07 June 2024. The methodological quality was assessed using the QUADAS-2 tool. Narrative synthesis of study results and heterogeneity was undertaken. Meta-analysis was not conducted due to the high variability in diagnostic thresholds. Results Fifteen out of 4099 identified studies met the inclusion criteria. Patient selection scored 'high' in risk of bias and applicability concerns. Examiner blinding was poorly reported. Sensitivity varied from 30% to 89%. Specificity varied from 41% to 100%. Heterogeneity was found across all studies in participant selection criteria, Tinel's test performance, electrodiagnostic criteria and diagnostic thresholds. Conclusions Tinel's test demonstrated variable diagnostic accuracy in CTS. Due to poor methodological quality and high variability among the studies, more DTA studies are necessary.

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ABSTRACT

Background

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Methods

Prospective studies evaluating Tinel's test in adults with CTS were included. The principal measures were sensitivity and specificity. A literature search was conducted for studies published up to 07 June 2024. The methodological quality was assessed using the QUADAS-2 tool. Narrative synthesis of study results and heterogeneity was undertaken. Meta-analysis was not conducted due to the high variability in diagnostic thresholds.

Results

Fifteen out of 4099 identified studies met the inclusion criteria. Patient selection scored 'high' in risk of bias and applicability concerns. Examiner blinding was poorly reported. Sensitivity varied from 30% to 89%. Specificity varied from 41% to 100%. Heterogeneity was found across all studies in participant selection criteria, Tinel's test performance, electrodiagnostic criteria and diagnostic thresholds.

Conclusions

Tinel's test demonstrated variable diagnostic accuracy in CTS. Due to poor methodological quality and high variability among the studies, more DTA studies are necessary.

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PROSPERO Protocol number: CRD42020218165 dated 27 November 2020.

INTRODUCTION

Carpal tunnel syndrome (CTS) is the symptomatic compression of the median nerve and the resultant chronic nerve inflammation within the fibro-osseous tunnel formed by the carpal bones and transverse carpal ligament [1]. It is the most common form of median nerve entrapment, representing 90% of all entrapment neuropathies [2].

Bilateral CTS accounts for approximately 60% of cases [3]. Symptoms, which occur in the median nerve distribution, include pain, numbness and paraesthesia that is usually worse at night and relieved by shaking of the hand(s) [4]. A cohort study of over 500,000 participants from the UK Biobank reported an overall CTS prevalence of 3.1% with a female preponderance [5]. An estimated one in 1000 individuals in the UK will undergo surgery for CTS every year [6]. In 2014-15 alone, CTS surgery cost the National Health Service in England £46 million [7]. This demonstrates the socio-economic impact of CTS.

Initial diagnosis is made based on symptom presentation, physical examination findings, questionnaires and electrodiagnostic tests [8]. Tinel's test is widely used by clinicians in primary care settings to support a diagnosis of suspected CTS [9]. A positive test produces paraesthesia and / or pain on percussion of the affected nerve along its distal sensory distribution [10]. The mechanism by which the test works and whether a positive test adds meaningful information to the diagnosis of nerve injury is not clear [11]. Tinel's test has shown validity in detecting nerve compromise in the superficially located tibial nerve in the tarsal tunnel [12]. In contrast, the median nerve has been shown to lie 6mm deep to line between the hook of hamate and trapezium tubercle [13]. This deeper anatomical location of median nerve may influence Tinel's test performance at the wrist.

Past systematic reviews have reported variable diagnostic test accuracy (DTA) for Tinel's test. Sensitivity ranged between 45-75% and specificity between 40-67% in one study [14]; and average values of 50% and 77% for sensitivity and specificity respectively, were reported in the other study [15]. Contemporary tools for assessing the methodological quality and risk of bias were not used in either study [16]. Further reviews have reported a sensitivity of 15-62% and specificity of 66-98% within an occupational setting [17], and pooled accuracy values of 55% and 75% for sensitivity and specificity respectively across different settings and including retrospective data [18]. The most recent review, which followed the PRISMA rather than PRISMA-DTA guidelines, did not define the study eligibility criteria and reference standard, and did not perform an assessment of risk of bias of the included studies [19]. Prospective studies of Tinel's test conducted within clinic settings have not been reviewed to date.

The primary objective of this review was to investigate the DTA of Tinel's test in detecting CTS among symptomatic adults seeking treatment in a healthcare setting. The secondary objective was to investigate factors contributing to heterogeneity between the studies in order to explain variations in DTA. The interpretation of the results when applying Tinel's test into clinical practice will be explored.

METHODS

The review was conducted in accordance with the protocol published in Prospero dated 27 November 2020, CRD42020218165. The findings are reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Cochrane DTA guidelines [16,20].

Eligibility Criteria

Participants: Participants were adults over the age of 18 years, who presented for diagnosis and treatment of CTS symptoms. The condition was defined based on the British Society of Surgery of the Hand (BSSH) guidelines as: '*All stages of insidious onset unilateral or bilateral CTS presented with altered sensation (tingling and numbness) in the thumb, index, middle and ring fingers, which are worse at night or first thing in the morning, clumsiness and associated pain in wrist and forearm and aggravated by gripping activities.'*
(https://www.bssh.ac.uk/patients/conditions/21/carpal_tunnel_syndrome)

Inclusion criteria: Prospective case control and non-case control studies of DTA of Tinel's test were included. Tinel's test or one of its pseudonyms (Tinel's sign, percussion test, Hoffmann-Tinel test/sign) was selected as the index test for CTS diagnosis. Electrodiagnosis was chosen as the reference standard (nerve conduction studies and/or electromyography). Primary, secondary, and tertiary health care centres settings were included.

Exclusion criteria: Epidemiological, population-based, longitudinal, retrospective studies as well as pre-employment screening in occupational settings were excluded. Studies were excluded if basic information on study setting, and age group were missing or there was insufficient information to complete two-by-two contingency tables.

Grouping: The principal diagnostic accuracy measures were sensitivity and specificity, related to the number of included participants or the number of included hands.

Information Sources

The following electronic databases were systematically searched from inception to 17 December 2020 and updated searches were undertaken on 7 June 2024: The Cochrane Library, MEDLINE (PubMed), Scopus, CINAHL plus and the Physiotherapy evidence base (PEDro). Google Scholar and Open Grey were searched for grey literature. The reference lists of the included studies were searched for further relevant literature.

Search terms included controlled terms (MeSH in PubMed), as well as free-text terms as index terms or free-text words. The broader search contained terms (including synonyms and closely related words): ('carpal tunnel syndrome' or 'median nerve entrapment' or 'median neuropathy') and ('Tinel' or 'Hoffmann' or 'percussion'). Only peer-reviewed articles were included. Conference abstracts were used to locate papers that were published in full text elsewhere but were excluded from the review. The search strategy and search results from PubMed for 7 June 2024 are provided in supplementary file 1.

Selection Process

All identified records were screened by two independent reviewers (SG, BK). The same two reviewers screened titles and abstracts and full reports and discussed these until agreement about inclusion/exclusion was reached. Throughout all stages a third reviewer (CML) was available if the two reviewers were unable to reach consensus about inclusion/exclusion for a study. The two reviewers reached consensuses for all studies and did not need to consult the third reviewer. For the full text article screen, reasons for exclusion per article were recorded. Data were extracted by SG and confirmed by CML and BK after addressing any discrepancies.

All references were exported to and managed using the reference management software, EndNote.

Data Collection Process and Data Items

The first author (SG) formulated a data extraction form based on the PRISMA-DTA item-checklist and performed data extraction [16,21]. This captured data on study design, study numbers, participant presentation, demographics, index and reference test description, diagnostic thresholds, information on risk of bias/study quality, number of true positives (TP), number of true negatives (TN), number of false positives (FP) and number of false negatives (FN).

Assessment of Risk of Bias and Methodological quality

The Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS-2) which is validated for use in DTA studies, was utilised for assessment of study quality and risk of bias [22]. Risk of bias was assessed in four domains including patient selection, index test, reference standard and flow and timing. Applicability concerns were assessed in the first 3 domains. The signalling questions in each domain was answered ‘yes’, ‘no’ or ‘unclear’ and the risk for each domain was judged as ‘low’, ‘high’ or ‘unclear’. The QUADAS-2 was trialled on 3 studies (SG), and then modified with signalling questions appropriate to the review prior to use on all included studies. For example, for the index test (Tinel’s) the signalling question was: ‘Was a pre-specified definition of a positive test provided?’. For the reference standard (electrodiagnosis), the signalling question was: ‘Was a protocol or guideline used?’, and ‘Was pre-specified cut-off values provided for a positive test?’. The risk of bias assessment was completed by SG and then independently verified by BK.

Data syntheses

Two-by-two diagnostic tables were constructed based on dichotomous data from the reference standard (positive or negative for CTS) and the index test (positive or negative for CTS as defined by each study). Summary forest plots were created with 95% confidence intervals (CI) for sensitivity and specificity for each study using Review Manager 5.4.1 (Review Manager, 2020). The review results were tabulated and summarised narratively. Individual study QUADAS-2 results were tabulated as recommended by Whiting et al. (2011) [22]. Narrative synthesis of study bias and heterogeneity were completed. The calculation of sensitivity and specificity summary values, a receiver-operating characteristic curve and meta-analysis was not performed due to high variability between studies, high levels of bias, and multiple diagnostic criteria and thresholds [23,24]. This also precluded a sensitivity analysis.

RESULTS

The flow of studies through the review process is illustrated in Figure 1.

A list of excluded studies is provided as supplementary file 2. A total of 3675 hands were included across 15 prospective studies. Eight studies used a case-control design. Study characteristics are summarised in table 1. The population was predominantly female with a mean age ranging between the 4th and 5th decade of life. Sample sizes ranged from 29 – 463 participants (Table 1). Table 2 summarises the criteria used by each study for suspected CTS, the method for performing Tinel's test and what constituted a positive test result. Table 3 summarises the neurophysiological thresholds used across 12 studies. Three studies did not report their diagnostic thresholds [25-27]; and 3 studies partially reported thresholds used

[28-30]. Thüngen et al. (2012) [28] based some results on repeated testing or on the neurophysiologists' opinion. The control groups did not undergo electrodiagnosis across 6 case-control studies [25,28-32].

Main review findings

A descriptive forest plot of Tinel's test DTA with numerical values for TP, FP, FN, TN, sensitivity, specificity and 95% CI's is presented in Figure 2. The degree of scatter was indicative of variability in sensitivity and specificity and wide CI's showed greater uncertainty.

There was contrasting results for the correlation of Tinel's test with CTS severity. Zhang et al. (2020) [26] showed positive correlation with moderate CTS, De Smet et al. (1995) [32] showed correlation with advanced CTS, whilst El Miedany et al. (2008) [34] demonstrated no correlation. De Smet et al. (1995) [32] found Tinel's test was more frequently positive in diabetics. Katz et al. (1990) [37] reported that over 55-year-olds with a positive Tinel's test combined with a probable or classic hand diagram had an 88.9% prevalence of CTS. Heller et al. (2008) [36] found a significant correlation between Tinel's test and electrodiagnosis (p <0.01). Kasundra et al., (2015) [25] reported the CTS questionnaire correlated better than Tinel's test with electrodiagnosis.

Risk of Bias and Methodological quality

Figure 3 summarises individual study QUADAS-2 results. Patient selection and flow and timing scored high for bias and applicability concerns. Poor reporting resulted in unclear judgements for the index and reference tests. Study designs which included healthy controls and lack of examiner blinding for the index and reference tests contributed to risk of bias. Inappropriate inclusion of participants who failed CTS

surgery, exclusion of co-morbid conditions, exclusion of participants who did not attend the reference test and those for whom the reference test provided an alternate diagnosis, further added to bias. There was lack of or limited methodological description of the index and reference tests. The time interval between receiving the index and reference tests and whether treatment was being offered during the time interval, were not disclosed. Applicability concerns were due to participant symptoms not being disclosed, participants not undergoing the index test or being excluded from the final analysis.

DISCUSSION

Summary of main results

Tinel's test sensitivity ranged from 30% (23%-37%) to 89% (85%-93%) and specificity ranged from 41% (35%-47%) to 100% (96%-100%). These results should be interpreted against the QUADAS-2 results for risk of bias and applicability concerns. Higher specificity was achieved when healthy controls were included, which is not representative of clinical practice. Small participant numbers in 12 (80%) of the 15 included studies may have led to inaccurate DTA, wide confidence intervals and insufficient levels of power and significance and may account for varied diagnostic accuracy for Tinel's test in this review. Whilst counting both hands for bilateral symptoms increases sample size, it is identified as a common error in medical studies as both hands may not be truly independent of each other [40].

Within this review, 11 (73%) studies did not report either participant-reported CTS severity or electrodiagnostic-rated CTS severity and 10 (66%) studies did not report

participant co-morbidities. This limited the interpretation of Tinel's test in relation to CTS severity and its performance in participants with co-morbid conditions. Some studies excluded participants with specific co-morbidities. This may be due to concerns that comorbidities would impact DTA estimates [41]. CTS is commonly associated with diabetes, thyroid disease, and pregnancy, and leads to significant morbidity [42-44]. The exclusion of such individuals who present with CTS symptoms may prove problematic as it excludes the application of Tinel's test to clinical practice where these individuals are likely to attend. The recommended exclusion criteria for CTS DTA studies are based on symptoms that fit other neurological disorders rather than on the existence of underlying conditions such as diabetes or thyroid disease [45]. The finding by De Smet et al. (1995) associating a more frequently positive Tinel's test with diabetes, echoed the findings of Jeong et al. (2014) [46] who compared clinical testing of CTS with and without diabetic neuropathy; however, the between-group difference was not statistically significant.

Sources of bias

The inclusion of either the more symptomatic hand or participants who failed CTS surgery, may disproportionately represent more severe cases which are easier to detect. This, together with the inclusion of asymptomatic controls, led to spectrum bias across the studies in this review [23,47]. The location in the referral pathway could have influenced the disease spectrum. The study setting included secondary and tertiary care clinics (table 2) that may usually see patients with more severe or 'difficult to diagnose' symptoms.

Across six case-control studies some participants did not undergo electrodiagnosis, leading to partial verification of the CTS diagnosis in those studies [47,48]. The

selection of electrodiagnosis as a reference standard may itself have led to bias (reference standard bias) [49,50]. Whilst CTS is a collection of signs and symptoms linked with small axon loss in Aδ and C-fibres as well as symptoms outside the median nerve distribution due to neuropathic input from the central nervous system [51-53], electrodiagnosis tests median neuropathy related to large, myelinated motor neurons and Aβ fibres [52,53]. Symptomatic individuals can return normal electrodiagnostic test values with a reported 16-34% of cases being missed [54,55]. For these reasons, electrodiagnosis cannot be considered as an error-free reference standard [50,56,57]. This makes it inherently problematic for DTA studies as sensitivity and specificity are dependent on a reliable reference standard [58,59].

In some instances, the exclusion of participants after the electrodiagnostic test provided an alternate diagnosis may have impacted the specificity of Tinel's test, which was proportionate to the number of participants without CTS [38,58]. These analysis-related biases could have been minimised by ensuring that all participants received both Tinel's test and electrodiagnosis and by the inclusion of all participants in the final analysis [60,61].

Sources of heterogeneity

The inclusion criteria for CTS symptoms were not consistently provided across all studies (Table 3). All but three studies described Tinel's test procedure but there was variability in the test performance, including the use of a reflex hammer versus digital tapping/percussion, and the number of strike repetitions (Table 3). Four studies did not provide a concise description of a positive Tinel's test [32,33,35,39], and a further three studies did not provide any description of a positive Tinel's test [25,30,36]. Many authors did not seek to reproduce pain when Tinel's test was performed (six

studies in this review included pain as a symptom, in addition to tingling and numbness). Although pain is not always present in CTS, it is an important feature of the condition [62]. The greatest disparity was found in both the number of electrodiagnostic criteria used and the diagnostic thresholds per criteria (Table 3), a finding that was consistent with the outcomes of a review on the sensitivity and specificity of NCS for the diagnosis of CTS by Demino and Fowler (2021) [63]. Whilst these factors may not directly impact study bias, it may influence comparability as varying test conditions may lead to different between-study results [47].

Regardless of the findings of this review, some authors have suggested that clinical tests as stand-alone tests have little merit [54,64]. Echoing this view, Tinel's test performed better when combined with other tests and when its diagnostic power was tested using alternative statistical methods. For example, Tinel's test sensitivity was shown to be 97% and specificity to be 91% in a retrospective study by Lajoie et al., (2005), in which the authors aimed to determine the sensitivity and specificity of common diagnostic tests for CTS using latent class analysis [65]. In another example, logistic regression demonstrated that Tinel's test combined with thenar weakness, Phalen's test and loss of 2-point discrimination significantly contributed to a diagnostic model for CTS, as shown in the study by Graham et al. (2006) [66].

Strengths and weaknesses of the review

PRISMA and Cochrane DTA guidelines were used to ensure transparent reporting. The study protocol was published on PROSPERO prior to undertaking the study. Methodological quality and bias were judged with a validated tool for DTA studies, the QUADAS-2. A robust search with a wide range of search terms across multiple databases was performed; however, the resources available to support this review

prevented the use of Embase for literature search. Grey literature searches of Google Scholar were conducted to reduce the risk of publication bias. Open Grey was added as an additional source of grey literature after submission of the protocol. Bias may have arisen from the exclusion of studies with insufficient data to calculate sensitivity and specificity, or those which did not state the setting and participant demographics. Attempts to obtain this information were not possible as author contact details were not disclosed.

Although it was the intention of this review to include primary care clinics, the setting was limited to secondary and tertiary clinics within the included studies. Low levels of reporting on participant selection criteria, examiner blinding, patient characteristics and electrodiagnostic test methods hindered the review results. For this reason, judgements were not made on diagnostic review bias and test review bias, which occur when examiners for the reference and index tests are not blinded [60].

The decision to exclude retrospective studies from the review was made to reduce potential recall and selection bias, however these studies may provide valuable information correlating Tinel's test with electrodiagnosis.

The choice of electrodiagnosis as the reference standard for CTS diagnosis may have limited the review results. Other diagnostic methods exist, including clinical diagnosis, magnetic resonance imaging and ultrasound [67], though was not within the scope of this review to explore other reference standards.

Meta-analysis was not performed due to the high levels of bias and heterogeneity. Narrative synthesis may be open to author interpretation [68].

IMPLICATIONS FOR PRACTICE

The usefulness of Tinel's test to the clinicians as a diagnostic tool for the diagnosis of CTS is not evident from the current literature. At least one study in this review suggested that Tinel's test was more sensitive and specific for wrist flexor tenosynovitis than for CTS [34]. At least in part, this lack of evidence is linked with the deficiencies in the published research.

In practice, the use of clinical tests does not replace a methodical approach to patient assessment and clinical reasoning. This review would suggest that if Tinel's test was the sole positive clinical test for CTS, clinicians should consider alternative differential diagnoses, particularly if patients do not respond as expected to usual treatment. Furthermore, in the absence of an accepted standard for performing Tinel's test, clinicians may improve the reliability of their own testing by ensuring that the same testing method is consistently followed.

Further research on the best method of applying Tinel's test would support its clinical application. For example, as the degree of median nerve compression varies between individuals from the wrist neutral posture up to 15° flexion or extension [69], altering the position of the wrist during testing could be explored. Additionally, as a recent study found that a timed Phalen's test of < 10 seconds was predictive of an abnormal nerve conduction test [70], a similar timed Tinel's test could be investigated.

The use of the Standards for Reporting of Diagnostic Accuracy Studies (STARD) 2015 guideline should help improve the quality and reporting of future studies [57]. Universal consensus on a CTS reference standard would provide consistency in test performance and diagnostic thresholds and allow for between-study comparisons and meta-analysis. Robust sample size estimation, statistical methods that account for inaccuracies in electrodiagnosis as a reference standard and correction methods

for missing data and dropouts should be planned at the study design stage [49,50,71].

CONCLUSIONS

This review found that the DTA of Tinel's test in CTS diagnosis of symptomatic adults was highly variable, as demonstrated by the broad range of sensitivity and specificity and wide CIs of the included studies. As identified, there were many limitations in the included studies. Many studies had small sample sizes, high levels of spectrum bias and applicability concerns on participant selection. Besides, the use of dissimilar electrodiagnostic criteria and diagnostic thresholds contributed to heterogeneity between studies, which in turn may have led to the variation in DTA. Overall, the transferability of the results to clinical practice was therefore limited. The consideration of alternate diagnoses would be prudent if Tinel's test was the sole positive clinical test for CTS in clinical practice. The authors recommend the need for more robust research to investigate the clinical usefulness of Tinel's test. Besides, further research is required to establish the anatomical structures that are targeted by Tinel's test and to explain the source of symptoms produced.

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Contributions of authors

SG and BK were responsible for the conception and design of the study. Both were also responsible for developing the search strategy. SG was responsible for

conducting the searches, screening, and rating the quality of papers, and data extraction, which were then verified by BK. All authors were responsible for the analysis and interpretation of the data. All authors contributed significantly to drafting or revising the manuscript critically for important intellectual content. All authors have approved the final version of this manuscript and agree to be accountable for all aspects of the work, its accuracy and integrity. The authors also confirm that all persons designated as authors qualify for authorship, and all those who qualify for authorship are listed. Requests for supportive data for this review should be made to the corresponding author (BK).

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TITLE PAGE

1. **Review title:** DIAGNOSTIC TEST ACCURACY OF TINEL'S TEST IN ADULTS WITH CARPAL TUNNEL SYNDROME – A SYSTEMATIC REVIEW.

2. **Keywords:** Carpal tunnel syndrome; Tinel's test; Diagnostic test accuracy; Median nerve.

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ABSTRACT

Background

Tinel's test is commonly used in the diagnosis of carpal tunnel syndrome (CTS) despite its questionable diagnostic test accuracy (DTA). This systematic review investigated the DTA of Tinel's test in CTS using electrodiagnosis as the reference standard and explored the heterogeneity between included studies.

Methods

Prospective studies evaluating Tinel's test in adults with CTS were included. The principal measures were sensitivity and specificity. A literature search was conducted for studies published up to 07 June 2024. The methodological quality was assessed using the QUADAS-2 tool. Narrative synthesis of study results and heterogeneity was undertaken. Meta-analysis was not conducted due to the high variability in diagnostic thresholds.

Results

Fifteen out of 4099 identified studies met the inclusion criteria. Patient selection scored 'high' in risk of bias and applicability concerns. Examiner blinding was poorly reported. Sensitivity varied from 30% to 89%. Specificity varied from 41% to 100%. Heterogeneity was found across all studies in participant selection criteria, Tinel's test performance, electrodiagnostic criteria and diagnostic thresholds.

Conclusions

Tinel's test demonstrated variable diagnostic accuracy in CTS. Due to poor methodological quality and high variability among the studies, more DTA studies are necessary.

Key words: Carpal tunnel syndrome; Tinel's test; Diagnostic test accuracy; Median nerve.

PROSPERO Protocol number: CRD42020218165 dated 27 November 2020.

INTRODUCTION

Carpal tunnel syndrome (CTS) is the symptomatic compression of the median nerve and the resultant chronic nerve inflammation within the fibro-osseous tunnel formed by the carpal bones and transverse carpal ligament [1]. It is the most common form of median nerve entrapment, representing 90% of all entrapment neuropathies [2].

Bilateral CTS accounts for approximately 60% of cases [3]. Symptoms, which occur in the median nerve distribution, include pain, numbness and paraesthesia that is usually worse at night and relieved by shaking of the hand(s) [4]. A cohort study of over 500,000 participants from the UK Biobank reported an overall CTS prevalence of 3.1% with a female preponderance [5]. An estimated one in 1000 individuals in the UK will undergo surgery for CTS every year [6]. In 2014-15 alone, CTS surgery cost the National Health Service in England £46 million [7]. This demonstrates the socio-economic impact of CTS.

Initial diagnosis is made based on symptom presentation, physical examination findings, questionnaires and electrodiagnostic tests [8]. Tinel's test is widely used by clinicians in primary care settings to support a diagnosis of suspected CTS [9]. A positive test produces paraesthesia and / or pain on percussion of the affected nerve along its distal sensory distribution [10]. The mechanism by which the test works and whether a positive test adds meaningful information to the diagnosis of nerve injury is not clear [11]. Tinel's test has shown validity in detecting nerve compromise in the superficially located tibial nerve in the tarsal tunnel [12]. In contrast, the median nerve has been shown to lie 6mm deep to line between the hook of hamate and trapezium tubercle [13]. This deeper anatomical location of median nerve may influence Tinel's test performance at the wrist.

Past systematic reviews have reported variable diagnostic test accuracy (DTA) for Tinel's test. Sensitivity ranged between 45-75% and specificity between 40-67% in one study [14]; and average values of 50% and 77% for sensitivity and specificity respectively, were reported in the other study [15]. Contemporary tools for assessing the methodological quality and risk of bias were not used in either study [16]. Further reviews have reported a sensitivity of 15-62% and specificity of 66-98% within an occupational setting [17], and pooled accuracy values of 55% and 75% for sensitivity and specificity respectively across different settings and including retrospective data [18]. The most recent review, which followed the PRISMA rather than PRISMA-DTA guidelines, did not define the study eligibility criteria and reference standard, and did not perform an assessment of risk of bias of the included studies [19]. Prospective studies of Tinel's test conducted within clinic settings have not been reviewed to date.

The primary objective of this review was to investigate the DTA of Tinel's test in detecting CTS among symptomatic adults seeking treatment in a healthcare setting. The secondary objective was to investigate factors contributing to heterogeneity between the studies in order to explain variations in DTA. The interpretation of the results when applying Tinel's test into clinical practice will be explored.

METHODS

The review was conducted in accordance with the protocol published in Prospero dated 27 November 2020, CRD42020218165. The findings are reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and the Cochrane DTA guidelines [16,20].

Eligibility Criteria

Participants: Participants were adults over the age of 18 years, who presented for diagnosis and treatment of CTS symptoms. The condition was defined based on the British Society of Surgery of the Hand (BSSH) guidelines as: '*All stages of insidious onset unilateral or bilateral CTS presented with altered sensation (tingling and numbness) in the thumb, index, middle and ring fingers, which are worse at night or first thing in the morning, clumsiness and associated pain in wrist and forearm and aggravated by gripping activities.'*
(https://www.bssh.ac.uk/patients/conditions/21/carpal_tunnel_syndrome)

Inclusion criteria: Prospective case control and non-case control studies of DTA of Tinel's test were included. Tinel's test or one of its pseudonyms (Tinel's sign, percussion test, Hoffmann-Tinel test/sign) was selected as the index test for CTS diagnosis. Electrodiagnosis was chosen as the reference standard (nerve conduction studies and/or electromyography). Primary, secondary, and tertiary health care centres settings were included.

Exclusion criteria: Epidemiological, population-based, longitudinal, retrospective studies as well as pre-employment screening in occupational settings were excluded. Studies were excluded if basic information on study setting, and age group were missing or there was insufficient information to complete two-by-two contingency tables.

Grouping: The principal diagnostic accuracy measures were sensitivity and specificity, related to the number of included participants or the number of included hands.

Information Sources

The following electronic databases were systematically searched from inception to 17 December 2020 and updated searches were undertaken on 7 June 2024: The Cochrane Library, MEDLINE (PubMed), Scopus, CINAHL plus and the Physiotherapy evidence base (PEDro). Google Scholar and Open Grey were searched for grey literature. The reference lists of the included studies were searched for further relevant literature.

Search terms included controlled terms (MeSH in PubMed), as well as free-text terms as index terms or free-text words. The broader search contained terms (including synonyms and closely related words): ('carpal tunnel syndrome' or 'median nerve entrapment' or 'median neuropathy') and ('Tinel' or 'Hoffmann' or 'percussion'). Only peer-reviewed articles were included. Conference abstracts were used to locate papers that were published in full text elsewhere but were excluded from the review. The search strategy and search results from PubMed for 7 June 2024 are provided in supplementary file 1.

Selection Process

All identified records were screened by two independent reviewers (SG, BK). The same two reviewers screened titles and abstracts and full reports and discussed these until agreement about inclusion/exclusion was reached. Throughout all stages a third reviewer (CML) was available if the two reviewers were unable to reach consensus about inclusion/exclusion for a study. The two reviewers reached consensuses for all studies and did not need to consult the third reviewer. For the full text article screen, reasons for exclusion per article were recorded. Data were extracted by SG and confirmed by CML and BK after addressing any discrepancies.

All references were exported to and managed using the reference management software, EndNote.

Data Collection Process and Data Items

The first author (SG) formulated a data extraction form based on the PRISMA-DTA item-checklist and performed data extraction [16,21]. This captured data on study design, study numbers, participant presentation, demographics, index and reference test description, diagnostic thresholds, information on risk of bias/study quality, number of true positives (TP), number of true negatives (TN), number of false positives (FP) and number of false negatives (FN).

Assessment of Risk of Bias and Methodological quality

The Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS-2) which is validated for use in DTA studies, was utilised for assessment of study quality and risk of bias [22]. Risk of bias was assessed in four domains including patient selection, index test, reference standard and flow and timing. Applicability concerns were assessed in the first 3 domains. The signalling questions in each domain was answered ‘yes’, ‘no’ or ‘unclear’ and the risk for each domain was judged as ‘low’, ‘high’ or ‘unclear’. The QUADAS-2 was trialled on 3 studies (SG), and then modified with signalling questions appropriate to the review prior to use on all included studies. For example, for the index test (Tinel’s) the signalling question was: ‘Was a pre-specified definition of a positive test provided?’. For the reference standard (electrodiagnosis), the signalling question was: ‘Was a protocol or guideline used?’, and ‘Was pre-specified cut-off values provided for a positive test?’. The risk of bias assessment was completed by SG and then independently verified by BK.

Data syntheses

Two-by-two diagnostic tables were constructed based on dichotomous data from the reference standard (positive or negative for CTS) and the index test (positive or negative for CTS as defined by each study). Summary forest plots were created with 95% confidence intervals (CI) for sensitivity and specificity for each study using Review Manager 5.4.1 (Review Manager, 2020). The review results were tabulated and summarised narratively. Individual study QUADAS-2 results were tabulated as recommended by Whiting et al. (2011) [22]. Narrative synthesis of study bias and heterogeneity were completed. The calculation of sensitivity and specificity summary values, a receiver-operating characteristic curve and meta-analysis was not performed due to high variability between studies, high levels of bias, and multiple diagnostic criteria and thresholds [23,24]. This also precluded a sensitivity analysis.

RESULTS

The flow of studies through the review process is illustrated in Figure 1.

A list of excluded studies is provided as supplementary file 2. A total of 3675 hands were included across 15 prospective studies. Eight studies used a case-control design. Study characteristics are summarised in table 1. The population was predominantly female with a mean age ranging between the 4th and 5th decade of life. Sample sizes ranged from 29 – 463 participants (Table 1). Table 2 summarises the criteria used by each study for suspected CTS, the method for performing Tinel's test and what constituted a positive test result. Table 3 summarises the neurophysiological thresholds used across 12 studies. Three studies did not report their diagnostic thresholds [25-27]; and 3 studies partially reported thresholds used

[28-30]. Thüngen et al. (2012) [28] based some results on repeated testing or on the neurophysiologists' opinion. The control groups did not undergo electrodiagnosis across 6 case-control studies [25,28-32].

Main review findings

A descriptive forest plot of Tinel's test DTA with numerical values for TP, FP, FN, TN, sensitivity, specificity and 95% CI's is presented in Figure 2. The degree of scatter was indicative of variability in sensitivity and specificity and wide CI's showed greater uncertainty.

There was contrasting results for the correlation of Tinel's test with CTS severity. Zhang et al. (2020) [26] showed positive correlation with moderate CTS, De Smet et al. (1995) [32] showed correlation with advanced CTS, whilst El Miedany et al. (2008) [34] demonstrated no correlation. De Smet et al. (1995) [32] found Tinel's test was more frequently positive in diabetics. Katz et al. (1990) [37] reported that over 55-year-olds with a positive Tinel's test combined with a probable or classic hand diagram had an 88.9% prevalence of CTS. Heller et al. (2008) [36] found a significant correlation between Tinel's test and electrodiagnosis (p <0.01). Kasundra et al., (2015) [25] reported the CTS questionnaire correlated better than Tinel's test with electrodiagnosis.

Risk of Bias and Methodological quality

Figure 3 summarises individual study QUADAS-2 results. Patient selection and flow and timing scored high for bias and applicability concerns. Poor reporting resulted in unclear judgements for the index and reference tests. Study designs which included healthy controls and lack of examiner blinding for the index and reference tests contributed to risk of bias. Inappropriate inclusion of participants who failed CTS

surgery, exclusion of co-morbid conditions, exclusion of participants who did not attend the reference test and those for whom the reference test provided an alternate diagnosis, further added to bias. There was lack of or limited methodological description of the index and reference tests. The time interval between receiving the index and reference tests and whether treatment was being offered during the time interval, were not disclosed. Applicability concerns were due to participant symptoms not being disclosed, participants not undergoing the index test or being excluded from the final analysis.

DISCUSSION

Summary of main results

Tinel's test sensitivity ranged from 30% (23%-37%) to 89% (85%-93%) and specificity ranged from 41% (35%-47%) to 100% (96%-100%). These results should be interpreted against the QUADAS-2 results for risk of bias and applicability concerns. Higher specificity was achieved when healthy controls were included, which is not representative of clinical practice. Small participant numbers in 12 (80%) of the 15 included studies may have led to inaccurate DTA, wide confidence intervals and insufficient levels of power and significance and may account for varied diagnostic accuracy for Tinel's test in this review. Whilst counting both hands for bilateral symptoms increases sample size, it is identified as a common error in medical studies as both hands may not be truly independent of each other [40].

Within this review, 11 (73%) studies did not report either participant-reported CTS severity or electrodiagnostic-rated CTS severity and 10 (66%) studies did not report

participant co-morbidities. This limited the interpretation of Tinel's test in relation to CTS severity and its performance in participants with co-morbid conditions. Some studies excluded participants with specific co-morbidities. This may be due to concerns that comorbidities would impact DTA estimates [41]. CTS is commonly associated with diabetes, thyroid disease, and pregnancy, and leads to significant morbidity [42-44]. The exclusion of such individuals who present with CTS symptoms may prove problematic as it excludes the application of Tinel's test to clinical practice where these individuals are likely to attend. The recommended exclusion criteria for CTS DTA studies are based on symptoms that fit other neurological disorders rather than on the existence of underlying conditions such as diabetes or thyroid disease [45]. The finding by De Smet et al. (1995) associating a more frequently positive Tinel's test with diabetes, echoed the findings of Jeong et al. (2014) [46] who compared clinical testing of CTS with and without diabetic neuropathy; however, the between-group difference was not statistically significant.

Sources of bias

The inclusion of either the more symptomatic hand or participants who failed CTS surgery, may disproportionately represent more severe cases which are easier to detect. This, together with the inclusion of asymptomatic controls, led to spectrum bias across the studies in this review [23,47]. The location in the referral pathway could have influenced the disease spectrum. The study setting included secondary and tertiary care clinics (table 2) that may usually see patients with more severe or 'difficult to diagnose' symptoms.

Across six case-control studies some participants did not undergo electrodiagnosis, leading to partial verification of the CTS diagnosis in those studies [47,48]. The

selection of electrodiagnosis as a reference standard may itself have led to bias (reference standard bias) [49,50]. Whilst CTS is a collection of signs and symptoms linked with small axon loss in Aδ and C-fibres as well as symptoms outside the median nerve distribution due to neuropathic input from the central nervous system [51-53], electrodiagnosis tests median neuropathy related to large, myelinated motor neurons and Aβ fibres [52,53]. Symptomatic individuals can return normal electrodiagnostic test values with a reported 16-34% of cases being missed [54,55]. For these reasons, electrodiagnosis cannot be considered as an error-free reference standard [50,56,57]. This makes it inherently problematic for DTA studies as sensitivity and specificity are dependent on a reliable reference standard [58,59].

In some instances, the exclusion of participants after the electrodiagnostic test provided an alternate diagnosis may have impacted the specificity of Tinel's test, which was proportionate to the number of participants without CTS [38,58]. These analysis-related biases could have been minimised by ensuring that all participants received both Tinel's test and electrodiagnosis and by the inclusion of all participants in the final analysis [60,61].

Sources of heterogeneity

The inclusion criteria for CTS symptoms were not consistently provided across all studies (Table 3). All but three studies described Tinel's test procedure but there was variability in the test performance, including the use of a reflex hammer versus digital tapping/percussion, and the number of strike repetitions (Table 3). Four studies did not provide a concise description of a positive Tinel's test [32,33,35,39], and a further three studies did not provide any description of a positive Tinel's test [25,30,36]. Many authors did not seek to reproduce pain when Tinel's test was performed (six

studies in this review included pain as a symptom, in addition to tingling and numbness). Although pain is not always present in CTS, it is an important feature of the condition [62]. The greatest disparity was found in both the number of electrodiagnostic criteria used and the diagnostic thresholds per criteria (Table 3), a finding that was consistent with the outcomes of a review on the sensitivity and specificity of NCS for the diagnosis of CTS by Demino and Fowler (2021) [63]. Whilst these factors may not directly impact study bias, it may influence comparability as varying test conditions may lead to different between-study results [47].

Regardless of the findings of this review, some authors have suggested that clinical tests as stand-alone tests have little merit [54,64]. Echoing this view, Tinel's test performed better when combined with other tests and when its diagnostic power was tested using alternative statistical methods. For example, Tinel's test sensitivity was shown to be 97% and specificity to be 91% in a retrospective study by Lajoie et al., (2005), in which the authors aimed to determine the sensitivity and specificity of common diagnostic tests for CTS using latent class analysis [65]. In another example, logistic regression demonstrated that Tinel's test combined with thenar weakness, Phalen's test and loss of 2-point discrimination significantly contributed to a diagnostic model for CTS, as shown in the study by Graham et al. (2006) [66].

Strengths and weaknesses of the review

PRISMA and Cochrane DTA guidelines were used to ensure transparent reporting. The study protocol was published on PROSPERO prior to undertaking the study. Methodological quality and bias were judged with a validated tool for DTA studies, the QUADAS-2. A robust search with a wide range of search terms across multiple databases was performed; however, the resources available to support this review

prevented the use of Embase for literature search. Grey literature searches of Google Scholar were conducted to reduce the risk of publication bias. Open Grey was added as an additional source of grey literature after submission of the protocol. Bias may have arisen from the exclusion of studies with insufficient data to calculate sensitivity and specificity, or those which did not state the setting and participant demographics. Attempts to obtain this information were not possible as author contact details were not disclosed.

Although it was the intention of this review to include primary care clinics, the setting was limited to secondary and tertiary clinics within the included studies. Low levels of reporting on participant selection criteria, examiner blinding, patient characteristics and electrodiagnostic test methods hindered the review results. For this reason, judgements were not made on diagnostic review bias and test review bias, which occur when examiners for the reference and index tests are not blinded [60].

The decision to exclude retrospective studies from the review was made to reduce potential recall and selection bias, however these studies may provide valuable information correlating Tinel's test with electrodiagnosis.

The choice of electrodiagnosis as the reference standard for CTS diagnosis may have limited the review results. Other diagnostic methods exist, including clinical diagnosis, magnetic resonance imaging and ultrasound [67], though was not within the scope of this review to explore other reference standards.

Meta-analysis was not performed due to the high levels of bias and heterogeneity. Narrative synthesis may be open to author interpretation [68].

IMPLICATIONS FOR PRACTICE

The usefulness of Tinel's test to the clinicians as a diagnostic tool for the diagnosis of CTS is not evident from the current literature. At least one study in this review suggested that Tinel's test was more sensitive and specific for wrist flexor tenosynovitis than for CTS [34]. At least in part, this lack of evidence is linked with the deficiencies in the published research.

In practice, the use of clinical tests does not replace a methodical approach to patient assessment and clinical reasoning. This review would suggest that if Tinel's test was the sole positive clinical test for CTS, clinicians should consider alternative differential diagnoses, particularly if patients do not respond as expected to usual treatment. Furthermore, in the absence of an accepted standard for performing Tinel's test, clinicians may improve the reliability of their own testing by ensuring that the same testing method is consistently followed.

Further research on the best method of applying Tinel's test would support its clinical application. For example, as the degree of median nerve compression varies between individuals from the wrist neutral posture up to 15° flexion or extension [69], altering the position of the wrist during testing could be explored. Additionally, as a recent study found that a timed Phalen's test of < 10 seconds was predictive of an abnormal nerve conduction test [70], a similar timed Tinel's test could be investigated.

The use of the Standards for Reporting of Diagnostic Accuracy Studies (STARD) 2015 guideline should help improve the quality and reporting of future studies [57]. Universal consensus on a CTS reference standard would provide consistency in test performance and diagnostic thresholds and allow for between-study comparisons and meta-analysis. Robust sample size estimation, statistical methods that account for inaccuracies in electrodiagnosis as a reference standard and correction methods

for missing data and dropouts should be planned at the study design stage [49,50,71].

CONCLUSIONS

This review found that the DTA of Tinel's test in CTS diagnosis of symptomatic adults was highly variable, as demonstrated by the broad range of sensitivity and specificity and wide CIs of the included studies. As identified, there were many limitations in the included studies. Many studies had small sample sizes, high levels of spectrum bias and applicability concerns on participant selection. Besides, the use of dissimilar electrodiagnostic criteria and diagnostic thresholds contributed to heterogeneity between studies, which in turn may have led to the variation in DTA. Overall, the transferability of the results to clinical practice was therefore limited. The consideration of alternate diagnoses would be prudent if Tinel's test was the sole positive clinical test for CTS in clinical practice. The authors recommend the need for more robust research to investigate the clinical usefulness of Tinel's test. Besides, further research is required to establish the anatomical structures that are targeted by Tinel's test and to explain the source of symptoms produced.

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Response to Reviewers' Comments

Reviewer #1

- The article is well-researched and structured, providing a comprehensive review of the diagnostic accuracy of Tinel's test for CTS. The systematic approach and adherence to guidelines are commendable.
- The main areas for improvement include conciseness in certain sections, greater emphasis on practical implications for clinicians, and a more detailed discussion of the limitations.
  RESPONSE: The introduction and results have been further summarised to improve conciseness, and we have expanded further on practical implications for the clinicians. Further discussion of limitations of the review has been added.
- The introduction provides a comprehensive overview of Carpal Tunnel Syndrome (CTS), highlighting its prevalence, symptoms, and socio-economic impact. The focus on Tinel's test as a diagnostic tool for CTS is well-defined.
- The introduction could benefit from a more concise summary of the primary objectives to streamline the reader's understanding.
  RESPONSE: We have simplified and clarified the study objectives.
- Some citations are older; ensuring the inclusion of the most recent studies would strengthen the context.
  RESPONSE: The citations from the introduction have been updated and the explanatory text has been edited accordingly. An updated search of systematic reviews that included Tinel's test has been conducted and the results have been discussed in comparison to our review.
- The methods section is thorough and follows a systematic approach, adhering to established guidelines for diagnostic test accuracy (DTA) studies.
- The results section is detailed and systematically presented, with a clear narrative synthesis of findings.
- Some results sections are lengthy and could benefit from further summarization to enhance readability.
  RESPONSE: The results have been summarised to reduce lengthy descriptions. An additional table has been added summarising the performance of Tinel's test.
- The discussion effectively synthesizes the findings, identifying key issues such as variability in diagnostic criteria and methodological quality.

- Some points are repeated; a more concise discussion would improve readability.
  RESPONSE: The manuscript has been edited to avoid duplication of information between the results and discussion. The discussion section has now been edited to improve clarity between the main results, bias, and heterogeneity.
- Expanding on the implications for clinicians in the application of Tinel's test in routine practice would be valuable.
  RESPONSE: As noted above, we have expanded further on the clinical implications.
- The conclusion summarizes the key findings and reiterates the need for improved research methodologies.
- The conclusion could briefly highlight the most critical aspects of the review's impact on clinical practice.
  RESPONSE: The conclusion has now been edited with clinical implications based on the reviewers' findings.
- References and tables appear appropriate.

Reviewer #2

- Generally, the Introduction was well written, but there are a lot of references, and not a lot of detail - for example "Tinel's test has demonstrated a wide range of sensitivity and specificity in the diagnosis of CTS [17-19]. " You have three references supporting this statement, but no detail on what the variety of sensitivity and specificity are. The entire Introduction could do with a re-write to reduce the references and increase specifics.
  RESPONSE: The number of references within the introduction have been reduced and updated with more recent/relevant citations. Values for sensitivity and specificity have now been added. Attempt has been made to only include directly relevant references and to improve the detail provided in the introduction. Overall, there are 71 references in this manuscript; however, 15 of those are the 'included studies' in the review.
- Introduction - the aims/objectives need clarifying, also, what is meant by updated review? Have the authors published a similar review?
  RESPONSE: As per the earlier comment, the introduction has now been clarified. The authors have not published a previous review. The statement with 'updated review' has been removed. A clearer explanation and analysis are given referring to the previous reviews that

had been performed prior to the PRISMA-DTA guidelines being set and any new reviews that have been since found.

- Methods - your statement at the start of Results about PRISMA, and your Prospero registration should be the first item in the Methods.
  RESPONSE: This has been corrected and moved as the first item in the methods section.
- Methods - would it be feasible to update the search? I note the last databases were searched up to December 2020.
  RESPONSE: The searches have been updated to 07 June 2024.
- Results, Discussion, and Conclusion were acceptable (but could have been more concise - these sections were not an easy read and could be tightened up considerably).
  RESPONSE: We hear you! The results have been simplified and summarised. However, as a key aspect of this review was to look at heterogeneity and its contribution to variation in DTA, we felt it was important that the results section reflects how electrodiagnosis and Tinel's test were performed, and criteria used for diagnosis – this has therefore been added in a simple-to-read table. The discussion has been edited to avoid duplication of information and has been further summarised to improve conciseness.
- Table 2 – I expected to see the results of the studies (?). Have I missed something?
  RESPONSE: The results of the studies, i.e., DTA measures have been represented separately on a forest plot. Table 1 (previously named as table 2, we have now removed the search string and added this has a supplementary file) – this is a summary of the study characteristics only. We did not add the DTA results to this table to avoid duplication with the forest plot.
- Table 3 – I think you need to check the referencing here - it appears to be duplicated where you've named the study, then linked to the citation.
  RESPONSE: This has now been corrected; although please note that the referencing order has changed compared to the previous version.

Figure 1:

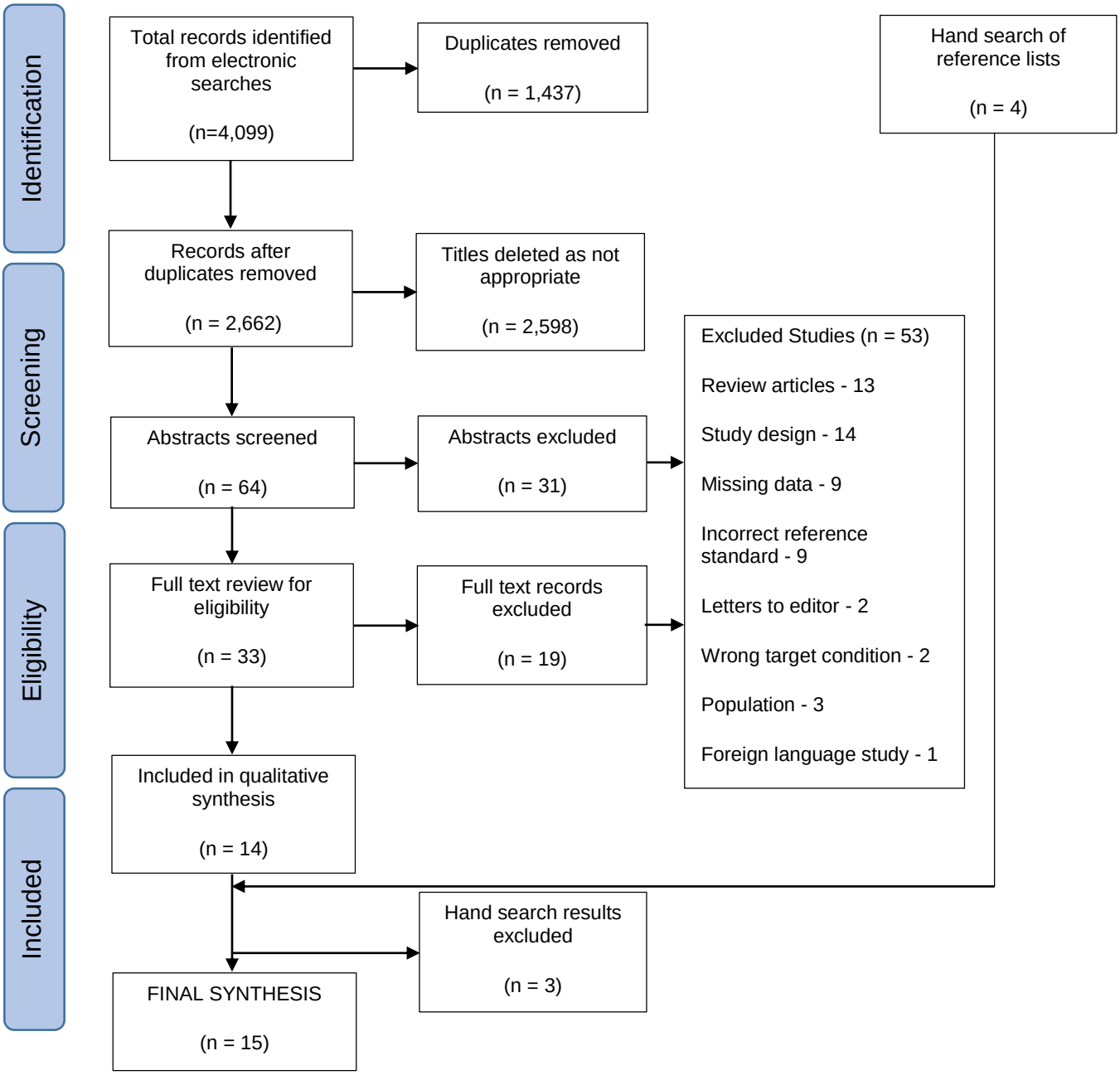

Figure 2:

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bruske 2002	99	32	48	68	0.67 [0.59, 0.75]	0.68 [0.58, 0.77]
Buch-Jaeger 1994	41	27	57	47	0.42 [0.32, 0.52]	0.64 [0.52, 0.74]
De Smet 1995	14	0	17	81	0.45 [0.27, 0.64]	1.00 [0.96, 1.00]
El Miedany 2008	55	17	129	31	0.30 [0.23, 0.37]	0.65 [0.49, 0.78]
Gerr 1998	8	13	49	168	0.14 [0.06, 0.26]	0.93 [0.88, 0.96]
Heller 1986	35	5	23	17	0.60 [0.47, 0.73]	0.77 [0.55, 0.92]
Kasundra 2015	73	2	20	21	0.78 [0.69, 0.86]	0.91 [0.72, 0.99]
Katz 1990	26	22	18	44	0.59 [0.43, 0.74]	0.67 [0.54, 0.78]
Kucukakkas 2019	202	140	24	97	0.89 [0.85, 0.93]	0.41 [0.35, 0.47]
Rayegani 2004	405	28	354	620	0.53 [0.50, 0.57]	0.96 [0.94, 0.97]
Tekeoglu 2007	37	0	13	50	0.74 [0.60, 0.85]	1.00 [0.93, 1.00]
Tetro 1998	70	9	25	87	0.74 [0.64, 0.82]	0.91 [0.83, 0.96]
Thungen 2012	19	1	30	2	0.39 [0.25, 0.54]	0.67 [0.09, 0.99]
Wiesman 2003	29	2	18	28	0.62 [0.46, 0.75]	0.93 [0.78, 0.99]
Zhang 2020	36	4	40	5	0.47 [0.36, 0.59]	0.56 [0.21, 0.86]

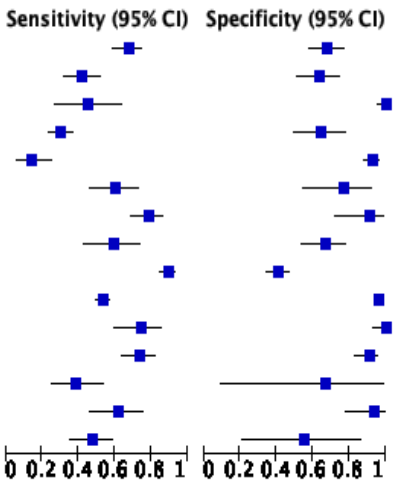

Figure 3:

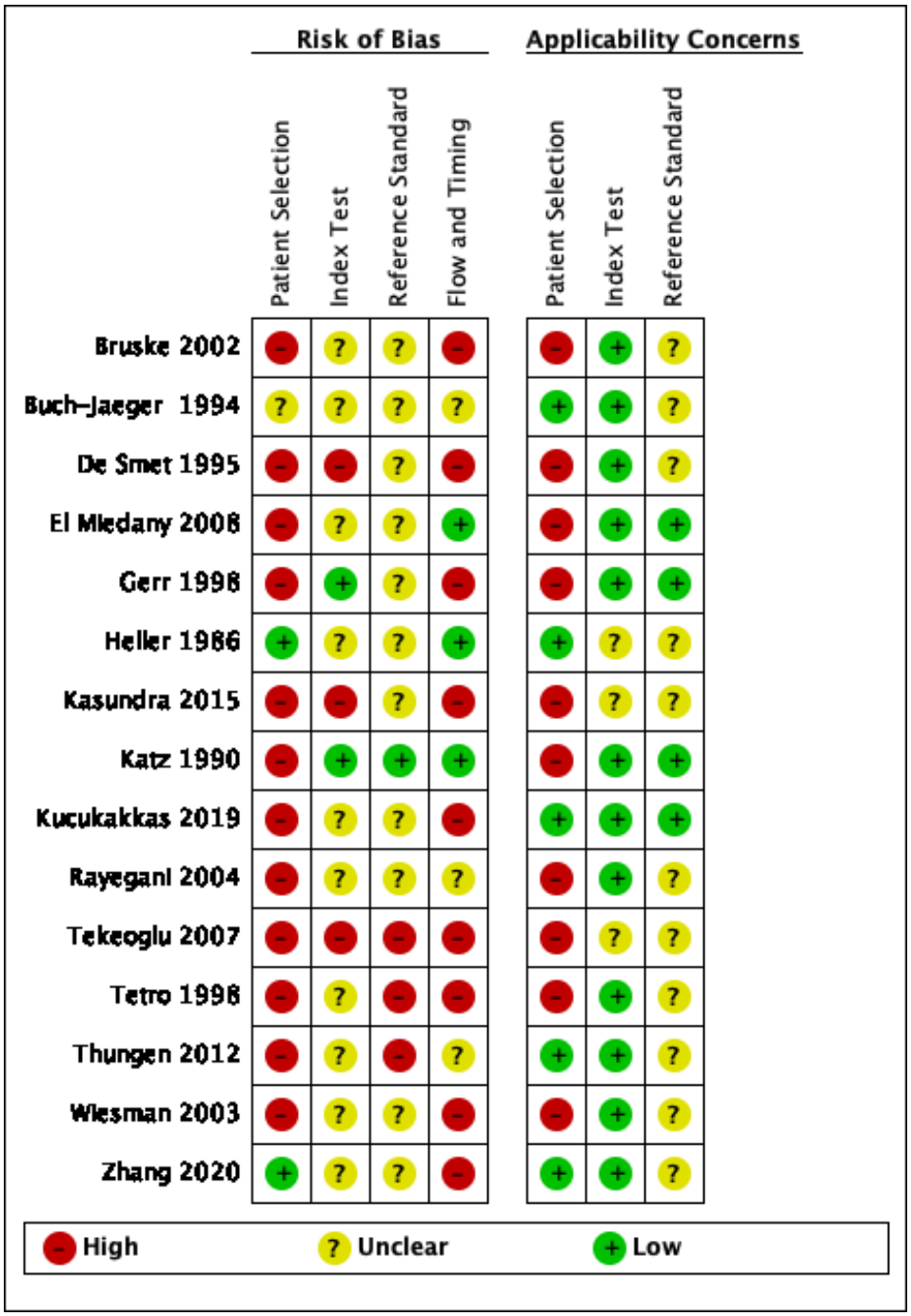
Risk of Bias
Applicability Concerns
Patient Selection
Index Test
Reference Standard
Flow and Timing
Patient Selection
Index Test
Reference Standard
Bruske 2002
Buch-Jaeger 1994
De Smet 1995
El Miedany 2008
Gerr 1998
Heller 1986
Kasundra 2015
Katz 1990
Kucukakkas 2019
Rayegani 2004
Tekeoglu 2007
Tetro 1998
Thungen 2012
Wiesman 2003
Zhang 2020
High
Unclear
Low

Figure captions & Alt-Text

Figure 1: PRISMA Study Flowchart.

Alt-Text: The PRISMA study flowchart describing how 15 studies were selected for inclusion in the review out of the 4,099 search results.

Figure 2: Paired forest plot of Tinel's Test DTA Results.

Alt-Text: Paired forest plot obtained from RevMan showing the sensitivity and specificity with 95% CI of 15 included studies.

Figure 3: QUADAS-2 Results Table.

Alt-Text: QUADAS-2 Results Table obtained from RevMan showing the risk of bias and applicability concern of 15 included studies. The risk is classified as high, unclear, or low.

Table 1: Summary of individual study characteristics.

Study	**Country**	**Setting:** CTS group	**Sample Size**		**CTS Group** Mean Age (Range)	**Control Group** Mean Age (Range)	**% of Females** CTS group (Control group)
			CTS Group Participant Number (Hands)	**Control Group** Participant number (Hands)			
Brüske 2004 [31]	Poland	Edx	112 (147)	50 (100)	53 (21-83)	36 (18-65)	79 (72)
Buch-Jaeger 1994 [33]	France	Edx	112 (172)	0	52 (29-81)	0	80
De Smet 1995 [32]	Belgium	Single surgeon practice	40 (54)	46 (81)	50.8 (23-77)	51 (34-76)	93 (100)
El Miedany 2008 [34]	Egypt	OPD	232	0	(20-91)	0	70
Gerr 1998 [35]	USA	Edx	(57)	(181)	50.1± 11.8	43.9± 12.6	83 (60)
Heller 1986 [36]	Israel	Edx	60 (80)	0	52 (F) 58 (M) (29-76)	0	82
Kasundra 2015 [25]	India	OPD neurology	54 (93)	20 (23)	43.9 ± 14	37 ± 16	85 (85)
Katz 1990 [37]	USA	Edx	110	0	46.6 ± 14.4	0	66
Küçükakkaş 2019 [38]	Turkey	OPD	463	0	46.7± 12 .7	0	79
Rayegani 2004 [39]	Iran	Medical centre Edx	436 (759)	324 (648)	45.2 ± 1 (23-75)	45.2 ± 3	91
Tekeoglu 2007 [30]	Turkey	OPD neurology	37 (50)	50	43.7 ± 10	41.2 ± 10	97 (98)
Tetro 1998 [29]	USA	Hospital referral	64 (65)	50 (96)	49.3 ± 14.6 (21-83.9)	46.9 ± 15 (22-79)	52 (74)
Thüngen 2012 [28]	Belgium	Hand clinic	49 (52)	0	52 (27-77)	0	82
Wiesman 2003 [27]	USA	Single	29 (47)	30	48 ± 10	45 ± 10	55 (57)

		surgeon practice					
Zhang 2020 [26]	USA	Single surgeon practice	55 (85)	0	59± 13	0	71

*Electrodiagnostic clinic (Edx); Outpatient clinic (OPD).

Table 2: CTS description, Tinel's test performance and criteria for a positive test.

Study	Symptom Description for the CTS Group	Test Method	Positive Test
Brüske 2004 [31]	Not reported.	Threefold percussion of palmer ligament region with a neurological hammer (mean force of hammer strike of 0.24kg) while maintaining a neutral wrist position.	Paraesthesia experienced in at least one of the 3 radial digits of the examined hand, in at least one of the three trials.
Buch-Jaeger 1994 [33]	Paraesthesia in the territory of the median nerve in the hand, occasional pain, nocturnal recrudescence of symptoms, numbness leading to clumsiness of the hand, with a mean symptom duration of 26 months.	Manual percussion of the volar surface of wrist.	Perceived paraesthesia.
De Smet 1995 [32]	Paraesthesia in median nerve distribution and an abnormal electrodiagnosis.	Manual tapping on the palmer aspect of the wrist.	The patient experienced paraesthesia.
El Miedany 2008 [34]	Paraesthesia, pain, swelling, weakness or clumsiness of the hand provoked or worsened by sleep / sustained hand or arm position, repetitive action of the hand or wrist that is mitigated by changing posture or by shaking the hand, sensory deficit or hypotrophy of the median innervated thenar muscle.	Percussion of the median nerve at the wrist.	Pain or numbness was reproduced in digits 1,2,3 (median nerve distribution).
Gerr 1998 [35]	Pain, weakness, numbness or tingling in the cutaneous distribution of the median nerve (thumb, index, long and ring finger) that involved either hand and occurring during the 2 weeks before enrolment in the study.	Percussion was performed bilaterally over the palmer aspect of the wrist with a standard reflex hammer.	Pain or paraesthesia that radiated into the hand.
Heller 1986 [36]	suspected CTS.	Not reported.	Not reported.

Kasundra 2015 [25]	Symptoms suggestive of CTS.	Not reported.	Not reported.
Katz 1990 [37]	Upper limb complaints.	The square end of a reflex hammer was dropped 5 times on the distal wrist crease from a height of 12cm.	Pain or paraesthesia was experienced in at least one finger innervated by median nerve.
Küçükakkaş 2019 [38]	Pain and paraesthesia in the median nerve distribution.	Tapping lightly long the wrist.	The presence of characteristic symptoms in median nerve sensation area.
Rayegani 2004 [39]	Pain and paraesthesia in the median nerve distribution	Percussing the median nerve at the wrist.	Paraesthesia reproduced.
Tekeoglu 2007 [30]	Nocturnal symptoms, thenar atrophy, abductor pollicis brevis changes.	Not reported.	Not reported.
Tetro 1998 [29]	Clinical symptoms of median nerve compression, typical history of pain or paraesthesia in the distribution of the median nerve, often worse at night and related to activity.	Gentle tapping over median nerve at wrist in neutral position.	The patient experienced paraesthesia or dysaesthesia in the distribution of the median nerve.
Thüngen 2012 [28]	Pain, tingling or numbness in the fingers innervated by the median nerve with usually nocturnal exacerbation of symptoms. The presence of symptoms in the adjacent territories to the median nerve, for example the fifth finger and the ulnar border of the fourth fingers, were not considered non-typical.	Gentle percussion of the median nerve above or at its passage within the carpal tunnel.	The appearance or exacerbation of paraesthesia or dysesthesia.
Wiesman 2003 [27]	Sensory alteration in median nerve distribution and abnormal nerve conduction across the carpal tunnel.	Applying four digital taps to the median nerve just proximal to the distal wrist crease.	Sensory alteration in median nerve distribution.
Zhang 2020 [26]	Clinically suspected CTS following a history taken by a fellowship-trained hand surgeon.	Percussion over the median nerve just proximal to the wrist crease. The author's included images of the examiner performing Tinel's test.	Paraesthesia was experienced distally in median nerve distribution.

Table 3: Electrodiagnostic criteria and diagnostic thresholds.

Criterion	Threshold	Study
Median sensory conduction velocity	< 40 to < 50 m/s	Brüske et al. (2004) [31], Buch-Jaeger et al. (1994) [33], De Smet et al. (1995) [32], El Miedany et al. (2008) [34], Gerr & Letz, (1998) [35], Katz et al. (1990) [37]
Median motor conduction velocity	< 49 m/s	El Miedany et al. (2008) [34]
Median DSL	> 3.5 to > 3.8 m/s	El Miedany et al. (2008) [34], Katz et al. (1990) [37], Gerr & Letz (1998) [35], Rayegani et al. (2004) [39]
Median DML	> 4.0 to > 4.5 m/s	Buch-Jaeger et al. (1994) [33], De Smet et al. (1995) [32], El Miedany et al. (2008) [34], Gerr & Letz (1998) [35], Heller et al. (1986) [36], Rayegani et al. (2004) [39], Thüngen et al. (2012) [28]
Median-ulna nerve peak sensory latency difference in ring finger	≥0.4 to ≥ 0.5 m/s	El Miedany et al. (2008) [34], Küçükakkaş et al. (2019) [38], Rayegani et al. (2004) [39], Tekeoglu et al. (2007) [30]
Median DML compared to contralateral side	≥0.5m/s	Tetro et al. (2007) [29]
Ipsilateral median-ulna nerve DML difference	≥1.8 m/s	Gerr & Letz (1998) [35]
Median mixed nerve palm-to-wrist latency	> 2.2m/s	Gerr & Letz (1998) [35]
APB (active or chronic) EMG abnormalities suggestive of denervation	≥0.5 m/s	Gerr & Letz (1998) [35]
Mixed peak latency palmer median-ulnar nerve difference	≥0.4 m/s	Küçükakkaş et al. (2019) [38]
Median-radial nerve peak sensory latency difference in 1st finger	≥0.5 m/s	Küçükakkaş et al. (2019 [38]

*distal sensory latency (DSL); distal motor latency (DML); abductor pollicis brevis (APB).

Supplementary File 1

SEARCH STRATEGY

Original searches conducted on: 20 December 2021.

Searches updated on: 07 June 2024

PubMed	**Search String**	**Records**
S1 Title/Abstract, Human, English	"Carpal tunnel syndrome" OR "median neuropathy" OR "median nerve entrapment" OR "median nerve compression"	10,926
S2 Title/Abstract, Human, English	"Tinel" OR "percussion" OR "Hoffmann*" OR "exam*" OR "test*" OR "clinical*" OR "provocat*" OR "screen*"	11,415,184
S3 Title/Abstract, Human, English	"electro*" OR "nerve conduct*" OR "neurophysiol*"	2,381,038
S4 Title/Abstract, Human, English	"diagnos*" OR "sensitivity" OR "specificity" OR "sensitivity and specificity" OR "predictive value" OR "odds ratio" OR "likelihood ratio" OR "ROC curve" OR "AUC"	4,647,512
S5	S1 AND S2 AND S3 AND S4	1,661

PEDro	**Search String**	**Records**
S1	"Carpal tunnel syndrome" OR "CTS"	276
CINAHL Plus	**Search String**	**Records**
Limiters – Human, English. Expanders – Apply equivalent subjects. Search modes – Boolean/Phrase.	("Carpal tunnel syndrome" OR "median neuropathy" OR "median nerve entrapment" OR "median nerve compression") AND ("Tinel" OR "percussion" OR "Hoffmann*" OR "exam*" OR "test*" OR "clinical*" OR "provocat*" OR "screen*") AND ("electro*" OR "nerve conduct*" OR "neurophysiol*") AND ("diagnos*" OR "sensitivity" OR "specificity" OR "sensitivity and specificity" OR "predictive value" OR "odds ratio" OR "likelihood ratio" OR "ROC curve" OR "AUC")	641
Scopus	**Search String**	**Records**

Limiters – Title/Abstract/Keywords, Human, English. Search modes – Boolean/Phrase. Expanders – Apply equivalent subjects.	(“Carpal tunnel syndrome” OR “median neuropathy” OR “median nerve entrapment” OR “median nerve compression”) AND (“Tinel” OR “percussion” OR “Hoffmann*” OR “exam*” OR “test*” OR “clinical*” OR “provocat*” OR “screen*”) AND (“electro*” OR “nerve conduct*” OR “neurophysiol*”) AND (“diagnos*” OR “sensitivity” OR “specificity” OR “sensitivity and specificity” OR “predictive value” OR “odds ratio” OR “likelihood ratio” OR “ROC curve” OR “AUC”)	703
Open Grey	**Search String**	**Records**
	(“Carpal tunnel syndrome” OR “median neuropathy” OR “median nerve entrapment” OR “median nerve compression”) AND (“Tinel” OR “percussion” OR “Hoffmann*” OR “exam*” OR “test*” OR “clinical*” OR “provocat*” OR “screen*”) AND (“electro*” OR “nerve conduct*” OR “neurophysiol*”) AND (“diagnos*” OR “sensitivity” OR “specificity” OR “sensitivity and specificity” OR “predictive value” OR “odds ratio” OR “likelihood ratio” OR “ROC curve” OR “AUC”)	7
Google Scholar	**Search String**	**Records**
	(“Carpal tunnel syndrome” OR “median neuropathy” OR “median nerve entrapment” OR “median nerve compression”) AND (“Tinel” OR “percussion” OR “Hoffmann*” OR “exam*” OR “test*” OR “clinical*” OR “provocat*” OR “screen*”) AND (“electro*” OR “nerve conduct*” OR “neurophysiol*”) AND (“diagnos*” OR “sensitivity” OR “specificity” OR “sensitivity and specificity” OR “predictive value” OR “odds ratio” OR “likelihood ratio” OR “ROC curve” OR “AUC”)	765
Cochrane Library	**Search String**	**Records**
Limiters – Title/Abstract/Keywords	(“Carpal tunnel syndrome” OR “median neuropathy” OR “median nerve entrapment” OR “median nerve compression”) AND (“Tinel” OR “percussion” OR “Hoffmann*” OR “exam*” OR “test*” OR “clinical*” OR “provocat*” OR “screen*”) AND (“electro*” OR “nerve conduct*” OR “neurophysiol*”) AND	46

	(“diagnos*” OR “sensitivity” OR “specificity” OR “sensitivity and specificity” OR “predictive value” OR “odds ratio” OR “likelihood ratio” OR “ROC curve” OR “AUC”)	
	Total Records	4,099

Supplementary File 2

REFERENCE LIST OF EXCLUDED STUDIES

STUDIES EXCLUDED AT ABSTRACT STAGE (*n* = 31)

Alfonso, M. I., & Dzwierzynski, W. (1998). Hoffman-Tinel sign. The realities. *Physical medicine and rehabilitation clinics of North America*, *9*(4), 721–v. Retrieved from https://pubmed.ncbi.nlm.nih.gov/9894091/

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STUDIES EXCLUDED AT FULL TEXT STAGE (n=19)

Campos-Serna, I., Garcia-Espinoza, J. A., Cahuana-Quispe, A. I., Marquez-Espriella, C., Cuervo-Vergara, M. A., Martinez-Lopez, J. C., & Dávila-Diaz, R. (2020). Diagnosis and Treatment of Carpal Tunnel Syndrome in A Tertiary Care Center in Mexico City. *World journal of plastic surgery*, *9*(2), 213–218. doi:10.29252/wjps.9.2.219

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STUDIES EXCLUDED AFTER HAND SEARCH (*n* = 3)

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REASONS FOR EXCLUSION

ABSTRACT STAGE

Reference	Reason for exclusion
Alfonso et al. (1998)	Review article
Almasi-Doghaee et al. (2016)	Letter to editor
Amo, C., et al. (1998)	Article in Spanish
Amirfeyz et al. (2011)	Electrodiagnosis not used as reference standard
Ansari et al. (2009)	Not DTA study
Bozek et al. (2001)	Correlational study
Cannon (2009)	Review article
Clark, C. B. (1988)	Letter to editor
Daras et al. (1987)	Review article
Davis et al. (2004)	Review article
Gelmers (1979)	Not DTA study
Ho et al. (2020)	Review article
Izadi et al. (2018)	Correlational statistics, Not DTA
Kanaan et al. (2001)	Review article
Kuschener et al. (1992)	Retrospective study
Lajoie et al. (2005)	Latent class analysis used, no reference standard
Lifchez et al. (2010)	Not DTA study
Martinez-Albaladejo et al. (1995)	Correlational study
Marx et al. (1998)	Not DTA study
Meder et al. (2012)	Review article
McCabe et al. (2010)	Case review article
Montagna et al. (2000)	Review
Novak et al. (1992)	Correlational study
Priganc et al. (2003)	Not DTA study
Radovic et al. (2014)	DTA tests not performed
Rentschler (1969)	Not specific to CTS
Rinkel et al. (2018)	Tinel’s sign tested on tibial nerve
Sansone et al. (2006)	Review article
Tinel’s and Phalen’s tests: what, why and how (2012)	Review series
Urbano et al. (2000)	Review
Walisinski (2017)	Review article

FULL TEXT STAGE

Reference	Reason for exclusion
Campos-Serna et al. (2020)	Retrospective epidemiological study of tertiary care centre
Faught (2001)	Use of combination gold standard – hand diagram classic/probable only and positive electrodiagnosis
Ghavanini et al. (1998)	Setting was unclear - 'laboratory' – not defined if this was a university study or care setting
Gellman et al. (1986)	No participant demographic data provided, specifically age group and gender. No author contacts details to request this information
Gonzalez del Pino et al. (1997)	Electrodiagnosis not used as reference standard
Hansen et al. (2004)	Age range starts under 18 years
Jeong et al. (2014)	Association between physical exam and electrodiagnosis performed but no standard DTA tests and no reported sensitivity or specificity. Electrodiagnosis not stated as reference standard as multiple linear regression analysis was used
Kuhlman et al. (1997)	No participant demographic data provided, specifically age group and gender. No author contacts details to request this information
MacDermid et al. (1997)	Reference standard used was combination of clinical diagnosis by hand surgeon and electrodiagnosis
Mossman et al. (1987)	Insufficient data – no details provided on patient selection and setting. No author contacts details provided.
Makanji et al. (2014)	Insufficient data to complete contingency table
Mondelli et al. (2001)	Age range started at 17 years for control group
Ntani et al. (2013)	Linear regression analysis used in diagnostic value of Tinel's sign.
Seror et al. (1987)	DTA tests were not performed, the study did not report sensitivity and specificity
Stewart & Eisen (1978)	Setting not specified
Szabo et al. (1999)	CTS group (I) was included on the basis of clinical presentation, clinical tests AND symptom relief from surgery
Walters & Rice (2002)	Data was collected retrospectively by reviewing records and then questioning clinicians on their clinical tests, test positivity and techniques

HAND SEARCH STAGE

Gelmers (1997)	Unable to confirm study setting and location in diagnostic pathway
Bowles et al. (1983)	Unable to confirm study setting and location in diagnostic pathway
Richter & Brüser (1999).	Unable to confirm study setting and location in diagnostic pathway