

Diagnosis and Treatment of Carpal Tunnel Syndrome

Progress Check

	Search	Title/Abstract	Full Text	Risk of Bias	Meta-Analysis	GRADE	Double-Check
Q1	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q2	Yes	Yes	Yes	Not Applicable	Not Applicable	Not Applicable	Not Applicable
Q3	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q4	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Q5	Yes	Yes	Yes	Not Applicable	Not Applicable	Not Applicable	Not Applicable
Q6	Yes	Yes	Yes	Not Applicable	Not Applicable	Not Applicable	Not Applicable
Q7	Yes	Yes	Yes	Not Applicable	Not Applicable	Not Applicable	Not Applicable
Q8	Yes	Yes	Yes	Yes	Yes	Yes	Yes

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Questions

Chapter 9: Diagnostic imaging

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Patients	with typical CTS history
Intervention/Diagnostics	High-resolution sonography
Control	only history-taking and clinical examination
Outcomes	Sensitivity and specificity

Question Q2

Patients	with typical CTS history
Intervention/Diagnostics	Magnetic resonance imaging of the hand
	If necessary, split according to MRI technique (MR neurography)
Control	only history taking and clinical examination
Outcomes	Sensitivity and specificity

Chapter 11.1: Conservative therapy

Question Q3

Patients	with confirmed CTS without neurological deficits (atrophy, numbness, paralysis) failure symptoms
Intervention	local infiltration of corticoid crystal suspension into the carpal tunnel under sonographic control
Control	local infiltration of corticoid crystal suspension into the carpal tunnel without sonographic control
Outcomes	 Primary Any clinical improvement (in accordance to the Cochrane Reviews) Secondary VAS BCTQ – SSS
	 BCTQ – FSS Complications/adverse effects Time to return to work

Question Q4

Patients	with confirmed CTS without neurological deficits
Intervention	low-level laser therapy
Control	Follow-up
Outcomes	Primary
	Any clinical improvement (in accordance to the Cochrane Reviews)
	Secondary
	• VAS

 BCTQ – SSS 	
DC1Q 333	

- BCTQ FSS
- Complications/adverse effects
- Time to return to work

Chapter 11.2: Surgical treatment

Question Q5

Patients	with confirmed CTS with neurological deficits with renal insufficiency requiring dialysis
Intervention	surgical treatment (all procedures)
Control	conservative treatment (all procedures)
Outcomes	PrimaryAny clinical improvement (in accordance to the Cochrane Reviews) Secondary
	 VAS BCTQ – SSS BCTQ – FSS Complications/adverse effects Time to return to work

Question Q6

Patients	with confirmed CTS with neurological deficits with breast cancer
Intervention	surgical treatment (all procedures)
Control	conservative treatment (all procedures)
Outcomes	Primary
	Any clinical improvement (in accordance to the Cochrane Reviews)
	Secondary
	• VAS
	BCTQ – SSS
	BCTQ – FSS
	 Complications/adverse effects
	Time to return to work

Question Q7

Patients	with radius fracture requiring surgical treatment and suspicious episodes of a CTS			
Intervention	surgical treatment (all procedures)			
Control	Follow-up (wait and see)			
Outcomes	Primary			
	• Any clinical improvement (in accordance to the Cochrane Reviews)			
	Secondary			
	• VAS			

•	BCTQ – SSS
•	BCTQ – FSS
•	Complications/adverse effects
•	Time to return to work

Question Q8

Patients	with confirmed CTS with neurological deficits					
Tatients	with committee C13 with heurological deficits					
Intervention	surgical treatment (all procedures) with tourniquet					
Control	surgical treatment (all procedures) in wide awake anesthesia					
Outcomes	Primary Any clinical improvement (in accordance to the Cochrane Reviews)					
	 Any clinical improvement (in accordance to the Cochrane Reviews) 					
	Secondary					
	 VAS BCTQ – SSS BCTQ – FSS Complications/adverse effects Time to return to work 					

Methods

We followed the Cochrane Handbook for Systematic Reviews of Interventions and Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy in designing and conducting the systematic reviews. We followed PRISMA reporting guidelines in reporting the final reviews.

Eligibility Criteria

Population

Although we considered patients with carpal tunnel syndrome with or without co-morbidities, sometimes the studies were including mixed population. If a study had mixed population and more than 50% of the participants had carpal tunnel syndrome, we included the study.

Intervention

We included the interventions regardless of their dosage and variations in administration. For steroid injection question, there were 2 studies that had 3 arms: 2 interventions and 1 control. Lee 2014 used ultrasound with inplane injection, outplane injection, and without ultrasound. We used the data from the inplane group as the intervention because that was more common across studies (5 other studies used inplane, 2 used outplane, and 3 did not report the technique). Rayegani 2019 used ultrasound with an ulnar site, a midline site, and without ultrasound. We used the data from the ulnar group because 9 of the other 10 studies used an ulnar site (and 1 did not report.)

Index Test

For index test (sonography) we included all CSA measures and sonography methods. We included Ultrasonography, Ultrasound, Sonography, High-Resolution Ultrasonography, High-Frequency Ultrasound, Power Doppler Ultrasonography, Color Doppler Sonography, Elastography, Shear Wave Elastography, and Superb Microvascular Imaging.

Reference Standard

Based on our agreement with clinical experts, we included all clinical assessment types as the reference standards and excluded any other form of diagnosis. The clinical assessments included physical examination, history taking, CTS-6, Two-point discrimination (2PD), Phalen, Tinel, and diagnostic criteria by American Academy of Neurology and American Academy of Orthopedic Surgeons.

Excluded Tests

We excluded Nerve Conduction, Electrodiagnostics, Electrophysiology, Electromyography, MRI, Diffusion Tensor Imaging, Electroneuromyography, Operations, VTIQ, Combination of any two tests, Neurography, Electromyelography, CT, and Ultrasomics.

Outcomes

We agreed on one primary outcome and four secondary outcomes based on consensus among five clinical experts. Although return to work was one of the outcomes, none of the studies reported data on this outcome. For Question on Laser Therapy, three studies reported that no complications were observed, and all of the other studies did not even mention complications.

Timepoints for Outcomes

For clinical outcomes of interventional systematic reviews, we considered these outcomes in a 3-month timepoint from the intervention. When a 3-month endpoint was not available, we used the nearest and longest available datapoint.

Endpoint Measures

Since the outcomes may be reported as change from baseline or endpoints, we followed the methods from relevant Cochrane reviews depending on the availability of the data.

Study Designs

We included randomised controlled trials for interventional questions and diagnostic test accuracy studies for diagnostic systematic review.

Search Methods

We searched Embase, MEDLINE, and Cochrane Library for all questions. The search strategies were designed and tested by an information scientist and peer-reviewed by another information scientist based on PRESS and PRISMA-S. Two members of clinical team commented and approved the search strategies before running the searches.

The searches were run in different dates so the search dates for each question was reported separately. We did not limit the search to language and publication date.

If we found any systematic review, we checked the list of their included studies to find more relevant studies.

Screening Methods

After de-duplication in EndNote X9, two members of team screened the titles and abstracts of search results using Rayyan.ai. We obtained the full texts for all the records that were included as relevant in title and abstract screening step. The full texts were screened by one reviewer and their decisions were shared with the clinicians for approval.

Data Management Methods

The data were extracted by three members of team. The extracted data included, PICOS information, risk of bias information, and quantitative data.

Interventional Studies

For international questions, we used the default data extraction form embedded in Reviewer Manager 5.4 (RevMan), including Cochrane's Risk of Bias tool. The entered data were analysed by RevMan.

When all the studies used the same measurement tool and scale, we used Mean Difference (MD) as effect size measure, and when they used different tools or scales, we used Standardised Mean Difference (SMD) so the data from studies could be combined. In almost all the cases for the questions we analysed, SMD was used because of different visual analogue scales across studies. For binary (dichotomous) outcomes, we used Risk Ratios (RR).

All of the continuous variables were analysed by comparing the actual value of the 3-month (or closest timepoint) outcome between the intervention and control groups. We did not compare the change between baseline and 3 months across groups, because most of the studies did not report the 3-month change with a standard deviation.

For choosing fixed effect vs. random effects, we followed the methods used by the Cochrane reviews. After entering the study data, we assessed the statistical heterogeneity. If $I^2>50\%$, we used a random effects model. If $I^2<50\%$ or if there was only a single study for that outcome (so heterogeneity did not apply), we used a fixed effect model. This approach is unrelated to the type of outcome (MD or SMD, dichotomous or continuous, same scale or different scale, etc.).

We used forest plots to visualise the meta-analysis results where intervention group was displayed in left and the control group at right side of the no-effect line. We used GRADE methodology for presenting the certainty of the evidence as explained by the Cochrane Handbook. Absolute effect estimates column in GRADE table displayed control group in right and the intervention group in left side of the column. We uploaded the RevMan files to MAGICapp and used MAGICapp for creating summary of findings table for interventional studies.

Diagnostic Test Accuracy Studies

We used Microsoft Access and Excel for data management. Sensitivities and specificities were abstracted as stated in the papers. Where available, 95% confidence intervals for the sensitivities and specificities were abstracted. Where not found, these were calculated manually using the figures in the papers. Data was imported into STATA 16. Using the meta-analysis window, forest plots and funnel plots were created. Random effects model was used because of heterogeneity in the studies. Sub-group analysis was also done by the type of test given.

The methodological quality of the included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool (Whiting 2011). The QUADAS-2 checklist consists of four domains, each of which is further divided into sub-items. Each item was scored as 'yes' (positive assessment, high quality), 'no' (negative assessment, low quality), or 'unclear'.

The certainty of the evidence was rated using GRADE methodology for diagnostic tests (GRADEpro 2015; Schünemann 2008; Singh 2012). Since MAGICapp does not support the creation of summary of findings table from diagnostic review, we used GRADEpro to create this table for diagnostic question. The five domains (risk of bias, indirectness, inconsistency, imprecision, and publication bias) as without concerns, with serious concerns, or with very serious concerns were judged. The assessment of the certainty of the evidence as high when studies were cross-sectional. For each of the five domains, the reason was judged as not serious, serious (downgraded by one level), or very serious (downgraded by two levels). The risk of bias was assessed using the QUADAS-2 tool. The indirectness in patient selection, index test, and reference standard were assessed using QUADAS-2 for concerns of applicability. Unexplained inconsistency was assessed whether it was present or not in sensitivity and

specificity estimates. Imprecision based on the width of the confidence intervals was also assessed. Publication bias was also assessed from the funnel plots.

Publication Bias

If the number of included studies in a meta-analysis was 10 or more, we used the funnel plot to assess the publication bias based on the plot's symmetry.

Quality Check

Extracted and analysed data from 25% of studies were double-check by an independent reviewer. This check resulted in two sensitivity analyses. The suggestions were not major and did not change the conclusion of the review

Search Strategies

Q1

Search Date: 13 October 2021

PubMed

(Carpal Tunnel Syndrome[MH] OR Carpal Tunnel Syndrome*[TIAB] OR Carpal Canal Syndrome*[TIAB] OR Thenar Amyotrophy of Carpal Origin[TIAB] OR Carpal Tunnel Median Neuropath*[TIAB] OR Carpal Tunnel Compression Neuropath*[TIAB] OR Carpal Tunnel Entrapment Neuropath*[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Brachialgia Paresthetica Nocturna[TIAB]) AND ("Ultrasonography"[MH:NoExp] OR "Ultrasonography, Doppler"[MH:NoExp] OR "Ultrasonography, Doppler, Duplex"[MH] OR "Ultrasonography, Doppler, Color"[MH] OR "Elasticity Imaging Techniques"[MH] OR Ultrasonogra*[TIAB] OR Ultrasound*[TIAB] OR Ultrasonic[TIAB] OR Sonogra*[TIAB] OR Echogra*[TIAB] OR Echoscop*[TIAB] OR Echosound[TIAB] OR Echotomogra*[TIAB] OR Elasticity Imaging*[TIAB] OR Elastogra*[TIAB] OR "Color Doppler"[TIAB] OR "Doppler Color"[TIAB] OR "Colour Doppler"[TIAB] OR "Doppler Colour"[TIAB] OR Vibro-Acoustograph*[TIAB] OR Sonoelastograph*[TIAB] OR Acoustic Radiation Force Impulse Imaging*[TIAB] OR ARFI[TIAB]) AND ("Sensitivity and Specificity"[MH] OR "Predictive Value of Tests"[MH] OR "ROC Curve"[MH] OR "False Negative Reactions"[MH] OR "False Positive Reactions"[MH] OR Sensitivitv[TIAB] OR Specificitv[TIAB] OR Diagnostic Accuracy[TIAB] OR Diagnostic Test Accuracy[TIAB] OR Diagnostic Performance[TIAB] OR ROC[TIAB] OR "Receiver Operating Characteristic"[TIAB] OR "Receiver Operating Characteristics"[TIAB] OR "Predictive Value"[TIAB] OR "Predictive Values"[TIAB] OR NPV[TIAB] OR NPVs[TIAB] OR PPV[TIAB] OR PPVs[TIAB] OR "False Positive" [TIAB] OR "False Negative" [TIAB] OR "True Positive"[TIAB] OR "True Negative"[TIAB]) 285

Embase via Ovid SP

Database: Embase <1974 to 2021 Week 40>

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- 2 Echography/ or Doppler Ultrasonography/ or Duplex Doppler Ultrasonography/ or Color Doppler Flowmetry/ or exp Elastography/ or (Ultrasonogra* or Ultrasound* or Ultrasonic or Sonogra* or Echogra* or Echoscop* or Echosound or Echotomogra* or Elasticity Imaging* or Elastogra* or (Colo?r adj Doppler) or (Doppler adj Colo?r) or Vibro-Acoustograph* or Sonoelastograph* or Acoustic Radiation Force Impulse Imaging* or ARFI).ti,ab. (799933)
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- 4 and/1-3 (437)
- 5 Limit 4 to embase (289)

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Search Date: 27 October 2021

PubMed

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- 2 Nuclear Magnetic Resonance Imaging/ or Diffusion Weighted Imaging/ or Echo Planar Imaging/ or Diffusion Tensor Imaging/ or (Chemical Shift Imaging* or "Diffusion Tensor" or Diffusion Tractogra* or "Echo Planar" or Echoplanar or Magnetic Resonance or Magnetization Transfer Contrast Imaging* or MR Tomogra* or MRI or MRIs or NMR or Proton Spin Tomogra* or "Spin Echo" OR Spinecho OR Magnetization Transfer Imaging* or Magnetization Transfer Imaging* or MR Imaging*).ti,ab. (1313828)
- 3 exp "Sensitivity and Specificity"/ or Predictive Value/ or Receiver Operating Characteristic/ or False Negative Result/ or False Positive Result/ or (Sensitivity or Specificity or (Diagnostic adj2 Accuracy) or (Diagnostic adj2 Performance) or ROC or Receiver Operating Characteristic? or Predictive Value? or NPV or NPVs or PPV or PPVs or False Positive or False Negative or True Positive or True Negative).ti,ab. (1909794)
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- 5 Limit 4 to embase (119)

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Search Date: 21 November 2021

PubMed

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- 2 Echography/ or Doppler Ultrasonography/ or Duplex Doppler Ultrasonography/ or Color Doppler Flowmetry/ or exp Elastography/ or (Ultrasonogra* or Ultrasound* or Ultrasonic or Sonogra* or Echogra* or Echoscop* or Echosound or Echotomogra* or Elasticity Imaging* or Elastogra* or (Colo?r adj Doppler) or (Doppler adj Colo?r) or Vibro-Acoustograph* or Sonoelastograph* or Acoustic Radiation Force Impulse Imaging* or ARFI).ti,ab. (806068)
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- 4 and/1-3 (312)
- 5 Limit 4 to embase (192)

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Date Run: 21/11/2021 13:50:42

#1 ([mh "Carpal Tunnel Syndrome"] OR (Carpal Tunnel Syndrome* OR Carpal Canal Syndrome* OR Thenar Amyotrophy of Carpal Origin OR Carpal Tunnel Median Neuropath* OR Carpal Tunnel Compression Neuropath*

OR Carpal Tunnel Entrapment Neuropath* OR Brachialgia Paraesthetica Nocturna OR Brachialgia Paresthetica Nocturna):ti,ab) AND ([mh ^Ultrasonography] OR [mh ^"Ultrasonography, Doppler"] OR [mh "Ultrasonography, Doppler, Duplex"] OR [mh "Ultrasonography, Doppler, Color"] OR [mh "Elasticity Imaging Techniques"] OR (Ultrasonogra* OR Ultrasound* OR Ultrasonic OR Sonogra* OR Echogra* OR Echoscop* OR Echosound OR Echotomogra* OR Elasticity Imaging* OR Elastogra* OR "Color Doppler" OR "Doppler Color" OR "Colour Doppler" OR "Doppler Colour" OR Vibro-Acoustograph* OR Sonoelastograph* OR Acoustic Radiation Force Impulse Imaging* OR ARFI):ti,ab) AND ([mh "Adrenal Cortex Hormones"] OR [mh Cortisone] OR [mh Glucocorticoids] OR [mh Hydroxycorticosteroids] OR [mh Ketosteroids] OR [mh Steroids] OR [mh Triamcinolone] OR [mh "Triamcinolone Acetonide"] OR [mh Methylprednisolone] OR [mh Betamethasone] OR (Adrenal Cortex Hormone* OR Corticosteroid* OR Corticoid* OR Cortisone OR Cortone Acetate OR Adreson OR Glucocorticoid* OR Glucorticoid* OR Triamcinolone OR "Tricort 40" OR Tricort40 OR Aristocort OR Volon OR Cinonide OR Kenalog OR Azmacort OR "Kenacort A" OR Methylprednisolone OR Metipred OR Urbason OR Medrol OR Cortisol OR Epicortisol OR Cortril OR Fludrocortisone OR Fluorocortisol OR Fludrohydrocortisone OR Hydroxycorticosterone OR Hydroxycortisone OR Fluorohydrocortisone OR Astonin OR FCOL OR Betamethasone OR Flubenisolone OR Betadexamethasone OR Celestona OR Celeston OR Celestone OR Hydroxycorticosteroid* OR Ketosteroid* OR Oxosteroid* OR Steroid*):ti,ab) 112

Q4

Search Date: 21 November 2021

PubMed

(Carpal Tunnel Syndrome[MH] OR Carpal Tunnel Syndrome*[TIAB] OR Carpal Canal Syndrome*[TIAB] OR Thenar Amyotrophy of Carpal Origin[TIAB] OR Carpal Tunnel Median Neuropath*[TIAB] OR Carpal Tunnel Compression Neuropath*[TIAB] OR Carpal Tunnel Entrapment Neuropath*[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Brachialgia Paresthetica Nocturna[TIAB] OR Lasers[MeSH] OR Lasers[TIAB] OR Lasers[TIAB] OR LLLT[TIAB] OR Photobiomodulation[TIAB] OR "Low-Level Light"[TIAB]) 113

Embase via Ovid SP

Database: Embase <1974 to 2021 Week 46>

- 1 Carpal Tunnel Syndrome* or Carpal Canal Syndrome* or Thenar Amyotrophy of Carpal Origin or Carpal Tunnel Median Neuropath* or Carpal Tunnel Compression Neuropath* or Carpal Tunnel Entrapment Neuropath* or Brachialgia Par?esthetica Nocturna).ti,ab. (17094)
- 2 exp Laser/ or exp Laser Therapy/ or (Laser OR Lasers OR LLLT OR Photobiomodulation OR "Low-Level Light").ti,ab. (335185)
- 3 and/1-2 (198)
- 4 Limit 3 to embase (157)

Cochrane Library (Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials=CENTRAL)

Date Run: 21/11/2021 14:51:00

#1 ([mh "Carpal Tunnel Syndrome"] OR (Carpal Tunnel Syndrome* OR Carpal Canal Syndrome* OR Thenar Amyotrophy of Carpal Origin OR Carpal Tunnel Median Neuropath* OR Carpal Tunnel Compression Neuropath* OR Carpal Tunnel Entrapment Neuropath* OR Brachialgia Paraesthetica Nocturna OR Brachialgia Paraesthetica Nocturna):ti,ab) AND ([mh Lasers] OR [mh "Laser Therapy"] OR (Laser OR Lasers OR LLLT OR Photobiomodulation OR "Low-Level Light"):ti,ab) 93

Search Date: 21 November 2021

PubMed

(Carpal Tunnel Syndrome[MH] OR Carpal Tunnel Syndrome*[TIAB] OR Carpal Canal Syndrome*[TIAB] OR Thenar Amyotrophy of Carpal Origin[TIAB] OR Carpal Tunnel Median Neuropath*[TIAB] OR Carpal Tunnel Compression Neuropath*[TIAB] OR Carpal Tunnel Entrapment Neuropath*[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Widney Insufficiency[mh] OR Renal Dialysis[MeSH] OR "Hemodialysis Units, Hospital"[MeSH] OR Kidney Failure*[TIAB] OR Kidney Injur*[TIAB] OR Kidney Insufficienc*[TIAB] OR Renal Failure*[TIAB] OR Renal Insufficienc*[TIAB] OR Chronic Kidney Disease*[TIAB] OR Chronic Renal Disease*[TIAB] OR End Stage Kidney Disease*[TIAB] OR End Stage Renal Disease*[TIAB] OR Dialysis[TIAB] OR Dialyses[TIAB] OR Hemodialysis[TIAB] OR Hemodialyses[TIAB] OR Hemodialysis[TIAB] OR Hemodialysis[TIAB] OR Haemodialyses[TIAB] OR Acetate Free Biofiltration*[TIAB]) AND ((Randomized Controlled Trial[PT] OR Controlled Clinical Trial[PT] OR Pragmatic Clinical Trial[PT] OR Randomized[TIAB] OR Randomised[TIAB] OR Placebo[TIAB] OR Randomly[TIAB] OR Trial[TIAB] OR Groups[TIAB]) NOT (Animals[MH]) NOT Humans[MH])) 64

Embase via Ovid SP

Database: Embase <1974 to 2021 Week 46>

- 1 Carpal Tunnel Syndrome* or Carpal Canal Syndrome* or Thenar Amyotrophy of Carpal Origin or Carpal Tunnel Median Neuropath* or Carpal Tunnel Compression Neuropath* or Carpal Tunnel Entrapment Neuropath* or Brachialgia Par?esthetica Nocturna).ti,ab. (17094)
- 2 exp Kidney Failure/ or exp Dialysis/ or (Kidney Failure* OR Kidney Injur* OR Kidney Insufficienc* OR Renal Failure* OR Renal Injur* OR Renal Insufficienc* OR Chronic Kidney Disease* OR Chronic Renal Disease* OR End Stage Kidney Disease* OR End Stage Renal Disease* OR Dialysis OR Dialyses OR Hemodialysis OR Hemodialyses OR Haemodialyses OR Hae
- 3 and/1-2 (835)
- 4 Limit 3 to embase (614)
- 8 Randomized controlled trial/ or Controlled clinical study/ or randomization/ or intermethod comparison/ or double blind procedure/ or human experiment/ or (random\$ or placebo or (open adj label) or ((double or single or doubly or singly) adj (blind or blinded or blindly)) or parallel group\$1 or crossover or cross over or ((assign\$ or match or matched or allocation) adj5 (alternate or group\$1 or intervention\$1 or patient\$1 or subject\$1 or participant\$1)) or assigned or allocated or (controlled adj7 (study or design or trial)) or volunteer or volunteers).ti,ab. or (compare or compared or comparison or trial).ti. or ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. (5570346)
- 6 (random\$ adj sampl\$ adj7 ("cross section\$" or questionnaire\$1 or survey\$ or database\$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.) (8758)
- 7 Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or (randomi?ed controlled or con
- 8 (((case adj control\$) and random\$) not randomi?ed controlled).ti,ab. (19113)
- 9 (Systematic review not (trial or study)).ti. (191167)
- 10 (nonrandom\$ not random\$).ti,ab. (17380)
- 11 ("Random field\$" or (random cluster adj3 sampl\$)).ti,ab. (3994)
- 12 (review.ab. and review.pt.) not trial.ti. (939739)
- 13 "we searched".ab. and (review.ti. or review.pt.) (38996)
- 14 ("update review" or (databases adj4 searched)).ab. (46509)

- 15 (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti. and animal experiment/ (1128199)
- 16 Animal experiment/ not (human experiment/ or human/) (2368121)
- 17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 (3825742)
- 18 5 not 17 (4940930)
- 19 4 and 18 (64)

Cochrane Library (Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials=CENTRAL)

Date Run: 21/11/2021 16:53:17

#1 ([mh "Carpal Tunnel Syndrome"] OR (Carpal Tunnel Syndrome* OR Carpal Canal Syndrome* OR Thenar Amyotrophy of Carpal Origin OR Carpal Tunnel Median Neuropath* OR Carpal Tunnel Compression Neuropath* OR Carpal Tunnel Entrapment Neuropath* OR Brachialgia Paraesthetica Nocturna OR Brachialgia Paraesthetica Nocturna):ti,ab) AND ([mh "Renal Insufficiency"] OR [mh "Renal Dialysis"] OR [mh "Hemodialysis Units, Hospital"] OR (Kidney Failure* OR Kidney Injur* OR Kidney Insufficienc* OR Renal Failure* OR Renal Injur* OR Renal Insufficienc* OR Chronic Kidney Disease* OR Chronic Renal Disease* OR End Stage Renal Disease* OR Dialysis OR Dialyses OR Hemodialysis OR Hemodialyses OR Haemodialyses OR Hemodialiteration* OR Acetate Free Biofiltration*):ti,ab) 22

Q6

Search Date: 21 November 2021

PubMed

(Carpal Tunnel Syndrome[MH] OR Carpal Tunnel Syndrome*[TIAB] OR Carpal Canal Syndrome*[TIAB] OR Thenar Amyotrophy of Carpal Origin[TIAB] OR Carpal Tunnel Median Neuropath*[TIAB] OR Carpal Tunnel Compression Neuropath*[TIAB] OR Carpal Tunnel Entrapment Neuropath*[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Breast Neoplasms[MeSH] OR Breast Cancer*[TIAB] OR Breast Neoplas*[TIAB] OR Breast Tumor*[TIAB] OR Breast Tumour*[TIAB] OR Breast Malignan*[TIAB] OR Mammary Cancer*[TIAB] OR Mammary Neoplas*[TIAB] OR Breast Carcinoma*[TIAB]) AND ((Randomized Controlled Trial[PT] OR Controlled Clinical Trial[PT] OR Pragmatic Clinical Trial[PT] OR Randomized[TIAB] OR Randomised[TIAB] OR Placebo[TIAB] OR Randomly[TIAB] OR Trial[TIAB] OR Groups[TIAB]) NOT (Animals[MH] NOT Humans[MH])) 12

Embase via Ovid SP

Database: Embase <1974 to 2021 Week 46>

- 1 Carpal Tunnel Syndrome* or Carpal Canal Syndrome* or Thenar Amyotrophy of Carpal Origin or Carpal Tunnel Median Neuropath* or Carpal Tunnel Compression Neuropath* or Carpal Tunnel Entrapment Neuropath* or Brachialgia Par?esthetica Nocturna).ti,ab. (17094)
- 2 Breast Tumor/ or exp Breast Cancer/ or (Breast Cancer* OR Breast Neoplas* OR Breast Tumor* OR Breast Tumour* OR Breast Malignan* OR Mammary Cancer* OR Mammary Carcinoma* OR Mammary Neoplas* OR Breast Carcinoma*).ti,ab. (639046)
- 3 and/1-2 (217)
- 4 Limit 3 to embase (182)
- Randomized controlled trial/ or Controlled clinical study/ or randomization/ or intermethod comparison/ or double blind procedure/ or human experiment/ or (random\$ or placebo or (open adj label) or ((double or single or doubly or singly) adj (blind or blinded or blindly)) or parallel group\$1 or crossover or cross over or ((assign\$ or match or matched or allocation) adj5 (alternate or group\$1 or intervention\$1 or patient\$1 or subject\$1 or participant\$1)) or assigned or allocated or (controlled adj7 (study or design or trial)) or volunteer or volunteers).ti,ab. or (compare or compared or comparison or trial).ti. or ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. (5570346)
- 6 (random\$ adj sampl\$ adj7 ("cross section\$" or questionnaire\$1 or survey\$ or database\$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.) (8758)
- 7 Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or (randomi?ed controlled or control group\$1).ti,ab.) (288287)
- 8 (((case adj control\$) and random\$) not randomi?ed controlled).ti,ab. (19113)
- 9 (Systematic review not (trial or study)).ti. (191167)
- 10 (nonrandom\$ not random\$).ti,ab. (17380)
- 11 ("Random field\$" or (random cluster adj3 sampl\$)).ti,ab. (3994)
- 12 (review.ab. and review.pt.) not trial.ti. (939739)
- "we searched".ab. and (review.ti. or review.pt.) (38996)
- 14 ("update review" or (databases adj4 searched)).ab. (46509)
- 15 (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti. and animal experiment/ (1128199)
- 16 Animal experiment/ not (human experiment/ or human/) (2368121)
- 17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 (3825742)
- 18 5 not 17 (4940930)

19 4 and 18 (48)

Cochrane Library (Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials=CENTRAL)

Date Run: 21/11/2021 17:16:58

#1 ([mh "Carpal Tunnel Syndrome"] OR (Carpal Tunnel Syndrome* OR Carpal Canal Syndrome* OR Thenar Amyotrophy of Carpal Origin OR Carpal Tunnel Median Neuropath* OR Carpal Tunnel Compression Neuropath* OR Carpal Tunnel Entrapment Neuropath* OR Brachialgia Paraesthetica Nocturna OR Brachialgia Paresthetica Nocturna):ti,ab) AND ([mh "Breast Neoplasms"] OR (Breast Cancer* OR Breast Neoplas* OR Breast Tumor* OR Breast Tumour* OR Breast Malignan* OR Mammary Cancer* OR Mammary Carcinoma* OR Mammary Neoplas* OR Breast Carcinoma*):ti,ab) 12

Search Date: 21 November 2021

PubMed

(Carpal Tunnel Syndrome[MH] OR Carpal Tunnel Syndrome*[TIAB] OR Carpal Canal Syndrome*[TIAB] OR Thenar Amyotrophy of Carpal Origin[TIAB] OR Carpal Tunnel Median Neuropath*[TIAB] OR Carpal Tunnel Compression Neuropath*[TIAB] OR Carpal Tunnel Entrapment Neuropath*[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Radius Fractures[MeSH] OR Hutchinson Fracture*[TIAB] OR Radius Distal Fracture*[TIAB] OR Radius Proximal Fracture*[TIAB] OR Radius Head Fracture*[TIAB] OR Radius Shaft Fracture*[TIAB] OR Chauffeur Fracture*[TIAB] OR Hutchinson Fracture*[TIAB] OR Radial Fracture*[TIAB] OR Colles Fracture*[TIAB] OR Barton Fracture*[TIAB] OR Galeazzi Fracture*[TIAB] OR Smith Fracture*[TIAB] OR Controlled Trial[PT] OR Controlled Clinical Trial[PT] OR Pragmatic Clinical Trial[PT] OR Randomized[TIAB] OR Randomised[TIAB] OR Placebo[TIAB] OR Randomly[TIAB] OR Trial[TIAB] OR Groups[TIAB]) NOT (Animals[MH] NOT Humans[MH])) 28

Embase via Ovid SP

Database: Embase <1974 to 2021 Week 46>

- 1 Carpal Tunnel Syndrome* or Carpal Canal Syndrome* or Thenar Amyotrophy of Carpal Origin or Carpal Tunnel Median Neuropath* or Carpal Tunnel Compression Neuropath* or Carpal Tunnel Entrapment Neuropath* or Brachialgia Par?esthetica Nocturna).ti,ab. (17094)
- 2 exp Radius Fracture/ or (Hutchinson Fracture* OR Radius Distal Fracture* OR Radius Proximal Fracture* OR Radius Head Fracture* OR Radius Shaft Fracture* OR Chauffeur Fracture* OR Hutchinson Fracture* OR Radial Fracture* OR Colles Fracture* OR Colles' Fracture* OR Barton Fracture* OR Galeazzi Fracture* OR Smith Fracture*).ti,ab. (12979)
- 3 and/1-2 (392)
- 4 Limit 3 to embase (316)
- Randomized controlled trial/ or Controlled clinical study/ or randomization/ or intermethod comparison/ or double blind procedure/ or human experiment/ or (random\$ or placebo or (open adj label) or ((double or single or doubly or singly) adj (blind or blinded or blindly)) or parallel group\$1 or crossover or cross over or ((assign\$ or match or matched or allocation) adj5 (alternate or group\$1 or intervention\$1 or patient\$1 or subject\$1 or participant\$1)) or assigned or allocated or (controlled adj7 (study or design or trial)) or volunteer or volunteers).ti,ab. or (compare or compared or comparison or trial).ti. or ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. (5570346)
- 6 (random\$ adj sampl\$ adj7 ("cross section\$" or questionnaire\$1 or survey\$ or database\$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.) (8758)
- 7 Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or (randomi?ed controlled or control group\$1).ti,ab.) (288287)
- 8 (((case adj control\$) and random\$) not randomi?ed controlled).ti,ab. (19113)
- 9 (Systematic review not (trial or study)).ti. (191167)
- 10 (nonrandom\$ not random\$).ti,ab. (17380)
- 11 ("Random field\$" or (random cluster adj3 sampl\$)).ti,ab. (3994)
- 12 (review.ab. and review.pt.) not trial.ti. (939739)
- 13 "we searched".ab. and (review.ti. or review.pt.) (38996)
- 14 ("update review" or (databases adj4 searched)).ab. (46509)
- 15 (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti. and animal experiment/ (1128199)
- 16 Animal experiment/ not (human experiment/ or human/) (2368121)

- 17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 (3825742)
- 18 5 not 17 (4940930)
- 19 4 and 18 (74)

Cochrane Library (Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials=CENTRAL)

Date Run: 21/11/2021 18:35:02

#1 ([mh "Carpal Tunnel Syndrome"] OR (Carpal Tunnel Syndrome* OR Carpal Canal Syndrome* OR Thenar Amyotrophy of Carpal Origin OR Carpal Tunnel Median Neuropath* OR Carpal Tunnel Compression Neuropath* OR Carpal Tunnel Entrapment Neuropath* OR Brachialgia Paraesthetica Nocturna OR Brachialgia Paresthetica Nocturna):ti,ab) AND ([mh "Radius Fractures"] OR (Hutchinson Fracture* OR Radius Distal Fracture* OR Radius Proximal Fracture* OR Radius Head Fracture* OR Radius Shaft Fracture* OR Chauffeur Fracture* OR Hutchinson Fracture* OR Radial Fracture* OR Colles Fracture* OR Colles' Fracture* OR Barton Fracture* OR Galeazzi Fracture* OR Smith Fracture*):ti,ab) 13

Search Date: 21 November 2021

PubMed

(Carpal Tunnel Syndrome[MH] OR Carpal Tunnel Syndrome*[TIAB] OR Carpal Canal Syndrome*[TIAB] OR Thenar Amyotrophy of Carpal Origin[TIAB] OR Carpal Tunnel Median Neuropath*[TIAB] OR Carpal Tunnel Compression Neuropath*[TIAB] OR Carpal Tunnel Entrapment Neuropath*[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] OR Brachialgia Paraesthetica Nocturna[TIAB] AND ("Tourniquets"[MH] OR Tourniquet*[TIAB] OR Artery Compression Device*[TIAB] OR External Fixator Vascular Compressor*[TIAB] OR External Vascular Compressor*[TIAB] OR Vascular Compression Device*[TIAB] OR Hysynal*[TIAB] OR ClampEase*[TIAB] OR ATS[TIAB] OR "A.T.S."[TIAB] OR "Io RACT"[TIAB] OR RadiStop*[TIAB] OR "TR Band"[TIAB] OR TRAcelet*[TIAB] OR Zephyr Vascular Compression Device*[TIAB]) AND ((Randomized Controlled Trial[PT] OR Controlled Clinical Trial[PT] OR Pragmatic Clinical Trial[PT] OR Randomized[TIAB] OR Randomised[TIAB] OR Placebo[TIAB] OR Randomly[TIAB] OR Trial[TIAB] OR Groups[TIAB]) NOT (Animals[MH] NOT Humans[MH])) 38

Embase via Ovid SP

Database: Embase <1974 to 2021 Week 46>

- 1 Carpal Tunnel Syndrome* or Carpal Canal Syndrome* or Thenar Amyotrophy of Carpal Origin or Carpal Tunnel Median Neuropath* or Carpal Tunnel Compression Neuropath* or Carpal Tunnel Entrapment Neuropath* or Brachialgia Par?esthetica Nocturna).ti,ab. (17094)
- 2 exp Tourniquet/ OR (Tourniquet* OR Artery Compression Device* OR External Fixator Vascular Compressor* OR External Vascular Compressor* OR Vascular Compression Device* OR Hysynal* OR ClampEase* OR ATS OR "A.T.S." OR "A.T.S." OR "Io RACT" OR RadiStop* OR "TR Band" OR TRAcelet* OR Zephyr Vascular Compression Device*).ti,ab. (20289)
- 3 and/1-2 (194)
- 4 Limit 3 to embase (128)
- Randomized controlled trial/ or Controlled clinical study/ or randomization/ or intermethod comparison/ or double blind procedure/ or human experiment/ or (random\$ or placebo or (open adj label) or ((double or single or doubly or singly) adj (blind or blinded or blindly)) or parallel group\$1 or crossover or cross over or ((assign\$ or match or matched or allocation) adj5 (alternate or group\$1 or intervention\$1 or patient\$1 or subject\$1 or participant\$1)) or assigned or allocated or (controlled adj7 (study or design or trial)) or volunteer or volunteers).ti,ab. or (compare or compared or comparison or trial).ti. or ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. (5570346)
- 6 (random\$ adj sampl\$ adj7 ("cross section\$" or questionnaire\$1 or survey\$ or database\$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.) (8758)
- 7 Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or (randomi?ed controlled or con
- 8 (((case adj control\$) and random\$) not randomi?ed controlled).ti,ab. (19113)
- 9 (Systematic review not (trial or study)).ti. (191167)
- 10 (nonrandom\$ not random\$).ti,ab. (17380)
- 11 ("Random field\$" or (random cluster adj3 sampl\$)).ti,ab. (3994)
- 12 (review.ab. and review.pt.) not trial.ti. (939739)
- 13 "we searched".ab. and (review.ti. or review.pt.) (38996)
- 14 ("update review" or (databases adj4 searched)).ab. (46509)
- 15 (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset\$1).ti. and animal experiment/ (1128199)
- 16 Animal experiment/ not (human experiment/ or human/) (2368121)

- 17 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 (3825742)
- 18 5 not 17 (4940930)
- 19 4 and 18 (41)

Cochrane Library (Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials=CENTRAL)

Date Run: 21/11/2021 19:06:50

#1 ([mh "Carpal Tunnel Syndrome"] OR (Carpal Tunnel Syndrome* OR Carpal Canal Syndrome* OR Thenar Amyotrophy of Carpal Origin OR Carpal Tunnel Median Neuropath* OR Carpal Tunnel Compression Neuropath* OR Carpal Tunnel Entrapment Neuropath* OR Brachialgia Paraesthetica Nocturna OR Brachialgia Paresthetica Nocturna):ti,ab) AND ([mh Tourniquets] OR (Tourniquet* OR Artery Compression Device* OR External Fixator Vascular Compressor* OR External Vascular Compressor* OR Vascular Compression Device* OR Hysynal* OR ClampEase* OR ATS OR "A.T.S." OR "A.T.S." OR "Io RACT" OR RadiStop* OR "TR Band" OR TRAcelet* OR Zephyr Vascular Compression Device*):ti,ab) 37

PRISMA Diagrams



Records identified through database searching (n=590)

Additional records identified through other sources (n=0)

Records after duplicates removed (n=403)



Screening

Records screened (n=403)

Records excluded (n=350)

with reasons

(n=37)

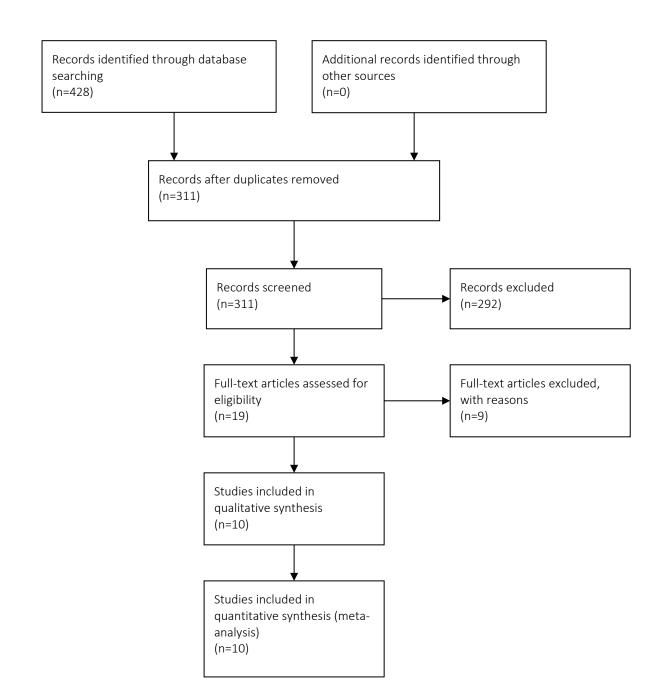
Full-text articles excluded,

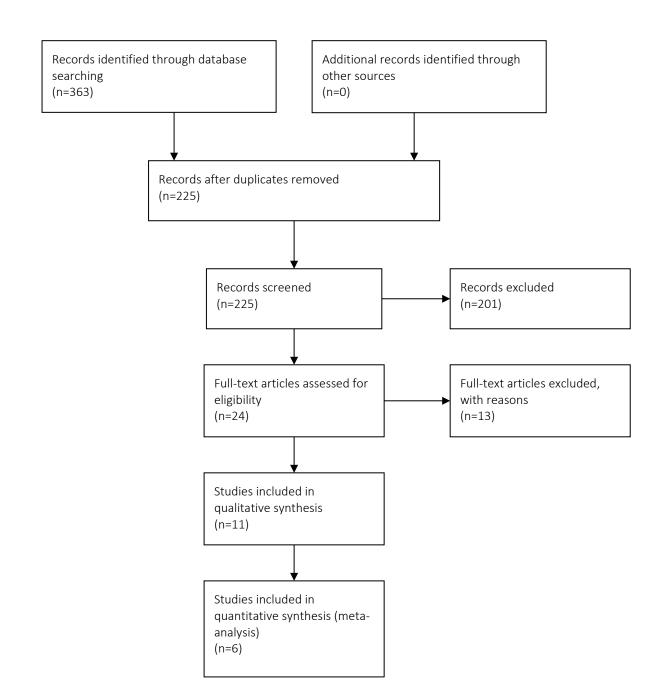
Full-text articles assessed for eligibility (n=53)

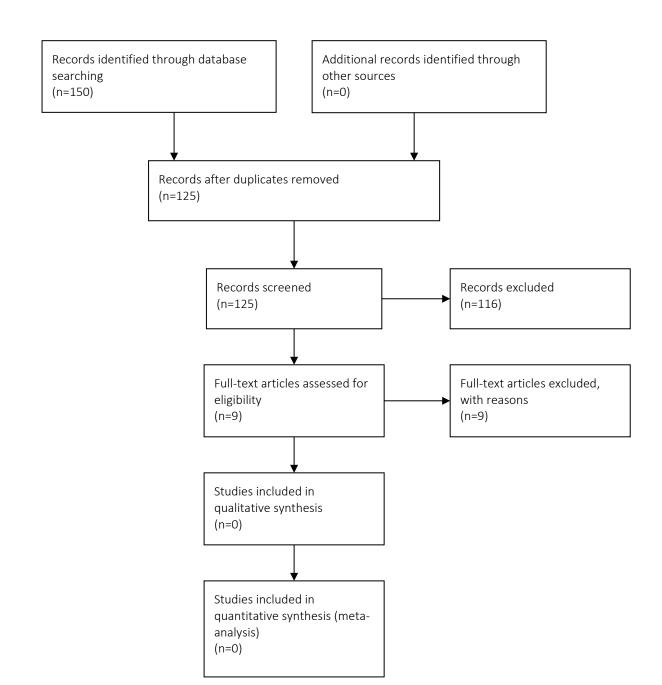
Studies included in qualitative synthesis (n=16)

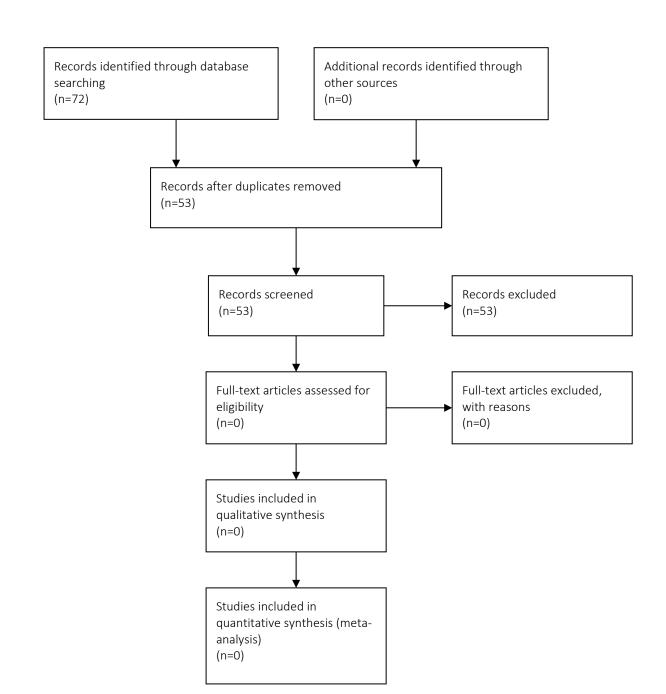
Studies included in quantitative synthesis (metaanalysis) (n=16)

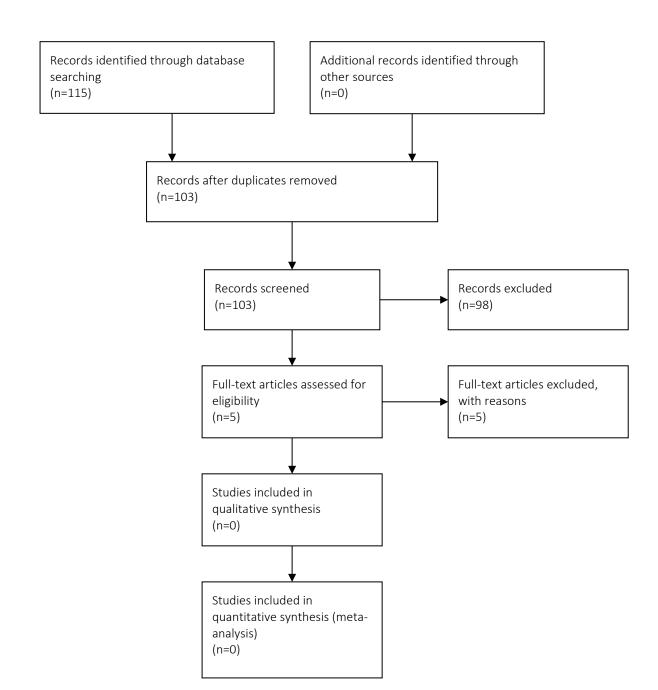
Eligibility

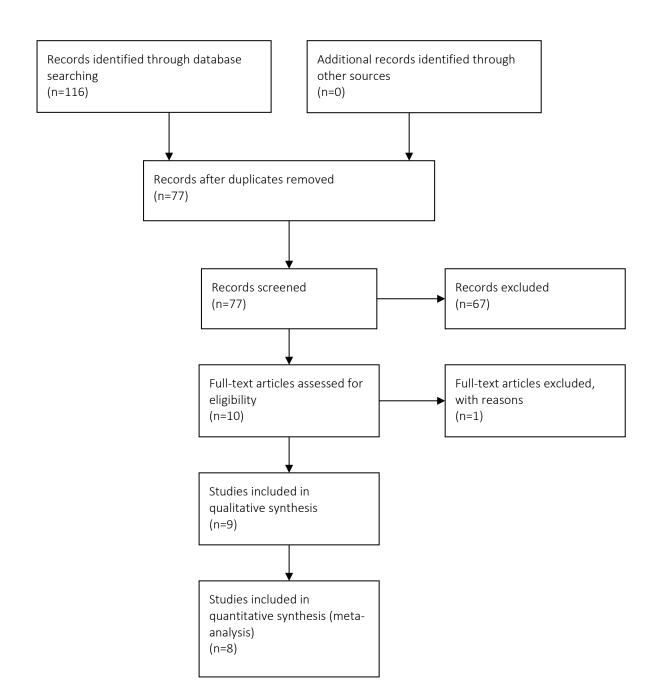










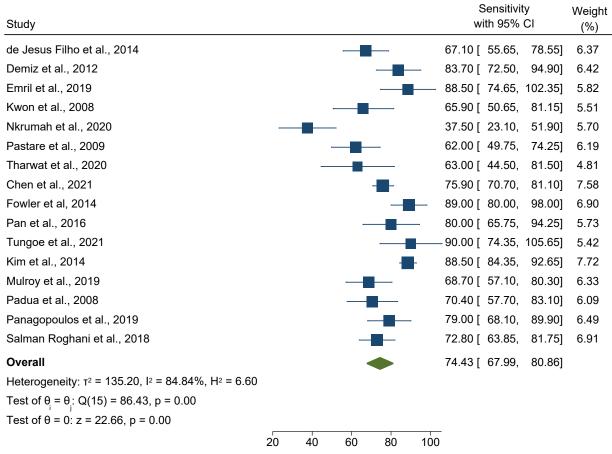


Meta-Analysis and Risk of Bias

Ω1

Assessment of Risk of Bias for Diagnostic Studies

	Risk of Bias		Applicability Concerns				
Study	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
de Jesus Filho et al., 2014	Low	Unclear	Low	Low	Low	Low	Low
Demiz et al., 2012	Low	Low	Low	Low	Low	Low	Low
Emril et al., 2019	Low	Low	Low	Low	Low	Low	Low
Kwon et al., 2008	Low	Low	Low	Low	Low	Low	Low
Nkrumah et al., 2020	High	Low	Low	Low	High	Low	Low
Pastare et al., 2009	Low	Low	Low	Low	Low	Low	Low
Tharwat et al., 2020	Low	Low	Low	Low	Low	Low	Low
Chen et al., 2021	Unclear	Low	Low	Low	Unclear	Low	Low
Fowler et al, 2014	Low	Low	Low	Low	Low	Low	Low
Pan et al., 2016	Low	Unclear	Low	Low	Low	Unclear	Low
Tungoe et al., 2021	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Kim et al., 2014	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear
Mulroy et al., 2019	Low	Low	Low	Low	Low	Low	Low
Padua et al., 2008	Low	Low	Low	Low	Low	Low	Low
Panagopoulos et al., 2019	Low	Low	Low	Low	Low	Low	Low
Salman Roghani et al., 2018	Low	Low	Low	Low	Low	Low	High



Random-effects REML model

Figure Q1-1 Forest plot for sensitivities

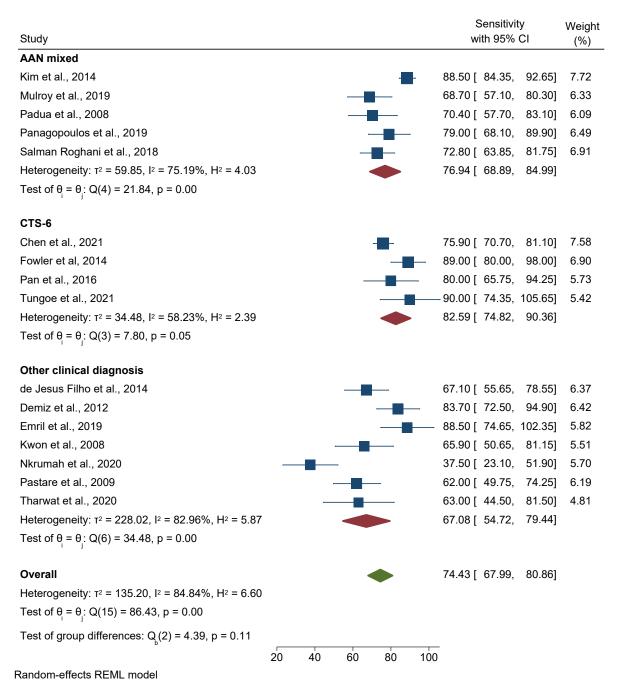
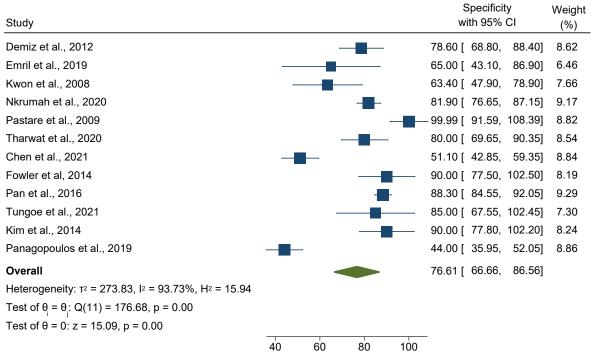
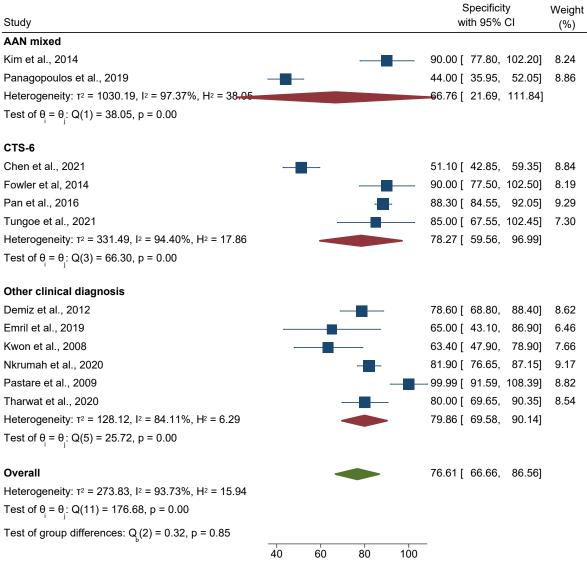


Figure Q1-2 Forest plot for sensitivities, stratified by type of diagnosis used



Random-effects REML model

Figure Q1-3 Forest plot for specificities



Random-effects REML model

Figure Q1-4 Forest plot for specificities, stratified by type of diagnosis used

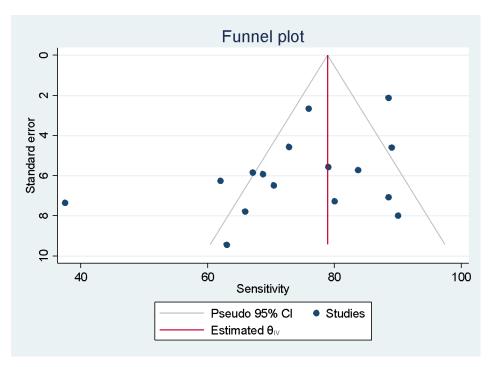


Figure Q1-5 Funnel plot for sensitivities to assess publication bias

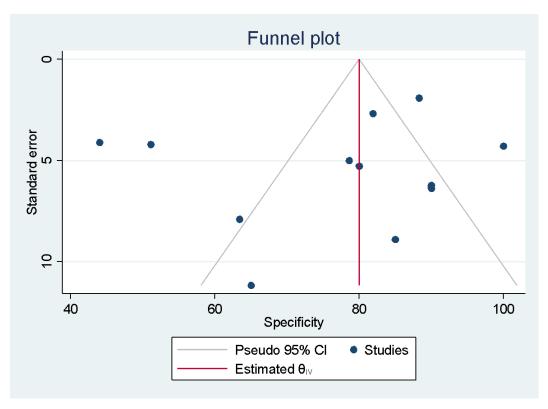


Figure Q1-6 Funnel plot for specificities to assess publication bias

Q1 Sensitivity analysis

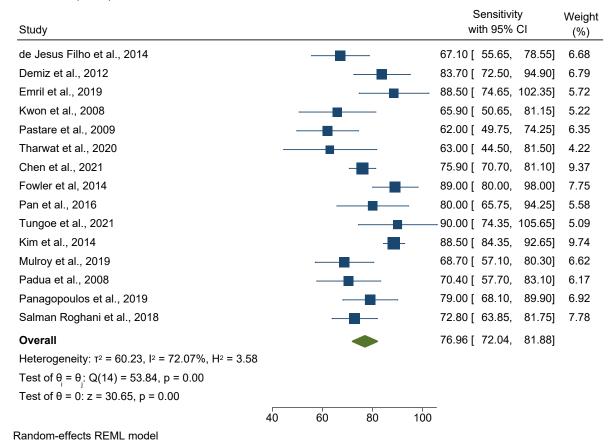


Figure Q1-7 Forest plot for sensitivity without Nkrumah 2020

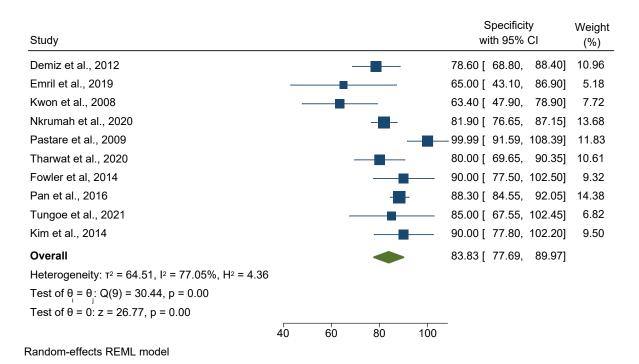


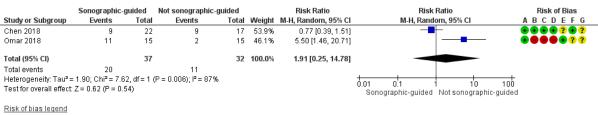
Figure Q1-8 Forest plot for specificity without Panagopoulos 2019 and Chen 2021

	Sonographic-g	uided	Not sonographic-gu	iided		Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	ABCDEFG
Makhlouf 2014	3	37	21	40	32.8%	0.15 [0.05, 0.48]		
Chen 2018	9	22	9	17	36.2%	0.77 [0.39, 1.51]		lacksquare
Omar 2018	11	15	2	15	31.0%	5.50 [1.46, 20.71]		
Total (95% CI)		74		72	100.0%	0.84 [0.15, 4.53]		
Total events	23		32					
Heterogeneity: Tau ² =	: 1.93; Chi ² = 16.3	37, df = 2	$(P = 0.0003); I^2 = 889$	%			0.01 0.1 1 10	100
Test for overall effect:	Z = 0.21 (P = 0.8	4)					Sonographic-guided Not sonographic-g	

Risk of bias legend

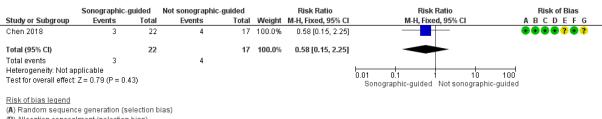
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
 (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias) (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q3-1: Any clinical improvement



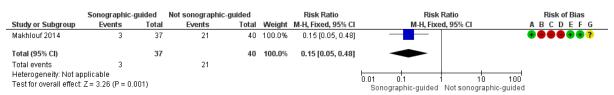
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias) (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q3-2: Clinical improvement: Numbness



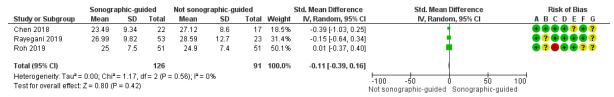
- (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q3-3: Clinical improvement: Hand weakness



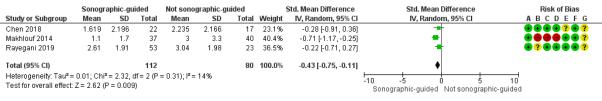
- (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q3-4: Clinical improvement: non-responder (2 cm or greater on VAS)



- Risk of bias legend (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias) (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q3-5: Clinical improvement: Grip strength

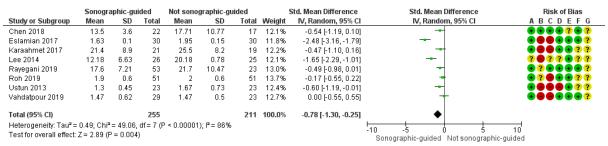


Risk of bias legend

- (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)

- (C) Blinding of participants and personnel (performance bias)
 (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
 (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q3-6: Pain (VAS)



- (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
 (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
 (F) Selective reporting (reporting bias)
- (G) Other bias

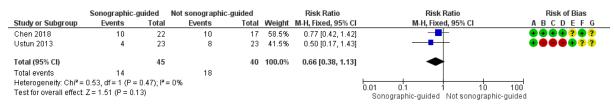
Figure Q3-7: BCTQ-SSS

	Sonogra	aphic-gu	ided	Not sonog	graphic-gui	ided	Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	ABCDEFG
Chen 2018	8.86	1.52	22	11.18	6.12	17	8.3%	-0.54 [-1.19, 0.10]		++++?+?
Eslamian 2017	1.54	0.97	30	1.61	0.12	30	13.4%	-0.10 [-0.61, 0.41]	+	
Karaahmet 2017	16.5	7.7	21	20	6.6	19	8.7%	-0.48 [-1.11, 0.15]		⊕ ⊕ ⊕
Lee 2014	8.76	3.86	26	10.18	7.14	25	11.3%	-0.24 [-0.80, 0.31]	 +	? \varTheta ? ? 👽 ? ?
Rayegani 2019	12.34	4.65	53	14.74	7.48	23	14.1%	-0.42 [-0.92, 0.07]		\bullet ? \bullet \bullet \bullet ?
Roh 2019	1.8	0.6	51	1.9	0.6	51	22.8%	-0.17 [-0.55, 0.22]	+	?+??
Ustun 2013	1.36	0.49	23	1.86	1.09	23	9.9%	-0.58 [-1.17, 0.01]		⊕ ⊕ ⊕
Vahdatpour 2019	1.39	0.6	29	1.37	0.53	23	11.5%	0.03 [-0.51, 0.58]	+	
Total (95% CI)			255			211	100.0%	-0.28 [-0.46, -0.09]	•	
Heterogeneity: Chi2=	4.43, df = 1	7 (P = 0.7)	$(3); I^2 = 0$	1%					t. t 1	
Test for overall effect:	Z = 2.93 (F	P = 0.003)						-10 -5 Ó 5 Sonographic-guided Not sonographic-	10 guided

Risk of bias legend

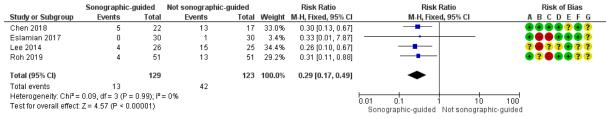
- (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
 (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias) (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q3-8: BCTQ-FSS



- Risk of bias legend
 (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias) (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q3-9: Complications: Pain



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias) (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias) (G) Other bias

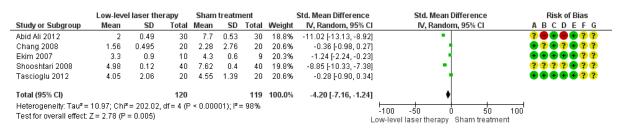
Figure Q3-10: Complications: Other

	Low-leve	l laser the	гару	Sharr	ıtreatır	ient		Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEFG
Chang 2008	21.19	4.12	20	17.38	3.56	20	24.8%	0.97 [0.31, 1.63]	•	\bullet ? \bullet ? \bullet ? ?
Ekim 2007	0.4	0.1	10	0.3	0.1	9	16.6%	0.96 [-0.01, 1.92]	•	lacksquare
Shooshtari 2008	22.86	5.13	40	21.52	6.05	40	32.6%	0.24 [-0.20, 0.68]	•	????•??
Tascioglu 2012	52.25	10.82	20	53.85	16.34	20	26.0%	-0.11 [-0.73, 0.51]	†	$\bullet \bullet \bullet \bullet \bullet ??$
Total (95% CI)			90			89	100.0%	0.45 [-0.05, 0.94]		
Heterogeneity: Tau ^z = Test for overall effect:			3 (P = 0	.06); I²=	: 59%				-50 -25 0 25 Sham therapy Low-level lase	50 r therapy

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias) (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

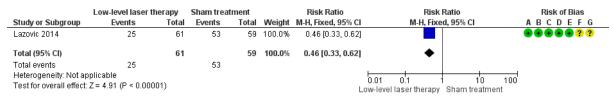
Figure Q4-1. Clinical Improvement: Grip Strength



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q4-2. Pain: Continuous



- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q4-3. Pain: Dichotomous

	Low-level laser therapy		Sham	Sham treatment			Mean Difference	Mean Difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEFG
Abid Ali 2012	21.8	2.8	30	37.2	4.4	30	35.5%	-15.40 [-17.27, -13.53]		? \varTheta 🖶 🖨 😯 ?
Chang 2008	19.35	0.63	20	28.71	0.85	20	37.2%	-9.36 [-9.82, -8.90]	•	\bullet ? \bullet ? \bullet ? ?
Ekim 2007	18	7	10	21	4	9	27.2%	-3.00 [-8.06, 2.06]	i †	$\bullet \bullet \bullet \bullet ??$
Total (95% CI)			60			59	100.0%	-9.77 [-14.86, -4.69]	· •	
Heterogeneity: $Tau^2 = 18.06$; $Chi^2 = 44.59$, $df = 2$ (P < 0.00001); $i^2 = 96\%$ Test for overall effect: $Z = 3.76$ (P = 0.0002)									-100 -50 0 50 Low-level laser therapy Sham treatn	100 nent

- Risk of bias legend

 (A) Random sequence generation (selection bias)

 (B) Allocation concealment (selection bias)

 (C) Blinding of participants and personnel (performance bias)

 (D) Blinding of outcome assessment (detection bias)

 (E) Incomplete outcome data (attrition bias)

 (F) Selective reporting (reporting bias)

 (G) Other bias

Figure Q4-4. BCTQ-SSS

	Low-level laser therapy		рy	Sham treatment				Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD T	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEFG
Abid Ali 2012	18.8	8	30	28.5	3.5	30	29.8%	-9.70 [-12.82, -6.58]	•	? • • • • ? ?
Chang 2008	11.04	0.43	20	19.6	1.02	20	41.0%	-8.56 [-9.05, -8.07]	•	$lackbox{0.5}{\bullet}$
Ekim 2007	14	4.2	10	17	3	9	29.1%	-3.00 [-6.26, 0.26]	•	$lackbox{0}$
Total (95% CI)			60			59	100.0%	-7.28 [-10.51, -4.05]	•	
Heterogeneity: $Tau^2 = 6.54$; $Chi^2 = 11.55$, $df = 2$ (P = 0.003); $I^2 = 83\%$ Test for overall effect: $Z = 4.42$ (P < 0.00001)								L	-100 -50 0 50 ow-level laser therapy Sham treatment	100

- Risk of bias legend

 (A) Random sequence generation (selection bias)

 (B) Allocation concealment (selection bias)

 (C) Blinding of participants and personnel (performance bias)

 (D) Blinding of outcome assessment (detection bias)

 (E) Incomplete outcome data (attrition bias)

 (F) Selective reporting (reporting bias)

 (G) Other bias

Figure Q4-5. BCTQ-FSS

	Tou	ırniqu	et	No to	urniqu	ıet	Std. Mean Difference		Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEFG
Braithwaite 1993	4.7	2.8	23	2.3	1.7	23	16.0%	1.02 [0.40, 1.64]	•	⊕ ? ⊕ ⊕ ? ?
Gunasagaran 2017	4.72	3.05	22	2.33	1.94	18	15.2%	0.90 [0.24, 1.55]	†	
lqbal 2018	4.6	2.59	36	2.8	2.59	37	19.5%	0.69 [0.21, 1.16]	<u>†</u>	• • ? ? • ? •
Lee 2020	7.38	1.67	22	4.28	1.37	22	13.6%	1.99 [1.26, 2.73]	•	$\bullet \bullet \bullet \bullet \bullet \bullet \bullet$
Okamura 2021	3.7	3.9	34	0.11	0.7	38	18.5%	1.30 [0.79, 1.81]	•	$lackbox{0} lackbox{0} lac$
Ralte 2010	3.4	5.63	25	0.2	5.63	25	17.2%	0.56 [-0.01, 1.13]	†	⊕ ? ● ? ● ●
Saleh 2021	3.58	0	36	1.68	0	31		Not estimable		$\bullet \bullet \bullet \bullet \bullet \bullet \bullet$
Total (95% CI)			198			194	100.0%	1.04 [0.67, 1.42]		
Heterogeneity: Tau² =	0.13; CI	ni² = 10	2.47, df	= 5 (P =	0.03)	; I² = 60	1%		-100 -50 0 50	100
Test for overall effect:	Z= 5.43	(P < 0	0.00001)					Favours tourniquet Favours no tour	

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

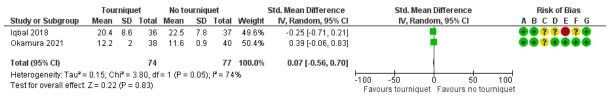
Figure Q8-1 Clinical improvement (Pain: Continuous)



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q8-2 Pain (dichotomous: VAS >4)



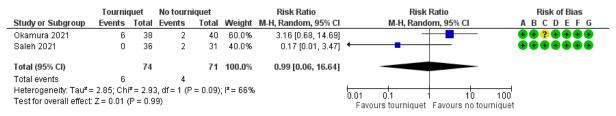
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias) (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q8-3 BCTQ-SSS

	Tou	rniqu	et	No to	urniqu	ıet	Std. Mean Difference		Std. Mean Difference Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI A B C D E F G
lqbal 2018	15.4	8.2	36	15.3	7.8	37	50.0%	0.01 [-0.45, 0.47]	
Okamura 2021	10.2	2.1	38	9	1.1	40	50.0%	0.71 [0.26, 1.17]	• • • • • • •
Total (95% CI)			74			77	100.0%	0.36 [-0.32, 1.05]	
Heterogeneity: $Tau^2 = 0.19$; $Chi^2 = 4.49$, $df = 1$ (P = 0.03); $I^2 = 78\%$ Test for overall effect: $Z = 1.04$ (P = 0.30)									-100 -50 0 50 100 Favours tourniquet Favours no tourniquet

- (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q8-4 BCTQ-FSS



- Risk of bias legend
 (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Figure Q8-5 Complications/adverse events

GRADE (Summary of Findings Table)

Q1

Question: Should sonography be used to diagnose carpal tunnel syndrome?

Sensitivity	0.77 (95% CI: 0.72 to 0.82)
Specificity	0.84 (95% CI: 0.78 to 0.90)

	№ of studies (№			Factors t	hat may decreas	se certainty of	evidence	Test accuracy
Outcome	of patients)	Study design	Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	CoE
True positives (patients with CTS)	15 studies 2260 patients ^a	cohort & case- control type studies	not serious	not serious	not serious	not serious	strong association	⊕⊕⊕ High
False negatives (patients incorrectly classified as not having CTS)								
True negatives (patients without CTS)	10 studies 1481 patients ^b	cohort & case- control type studies	not serious	not serious	not serious	not serious	publication bias strongly suspected strong association ^c	⊕⊕⊕ High
False positives (patients incorrectly classified as having CTS)							-	

Explanations

a. Patients in this case mean 'Number of wrists'; based on a systematic review of 15 studies: de Jesus Filho 2014, Demiz 2012, Emril 2019, Kwon 2008, Pastare 2009, Tharwat 2020, Chen 2021, Fowler 2014, Pan 2016, Tungoe 2021, Kim 2014, Mulroy 2019, Padua 2008, Panagopoulos 2019, Salman Roghani 2018;

b. Patients in this case mean 'Number of wrists'; based on a systematic review of 10 studies for true negatives and false positives: Demiz 2012, Emril 2019, Kwon 2008, Nkrumah 2020, Pastare 2009, Tharwat 2020, Fowler 2014, Pan 2016, Tungoe 2021, Kim 2014.

c. The funnel plot is indicative of publication bias

Q3
Intervention: Local infiltration of corticoid crystal suspension into the carpal tunnel under sonographic control
Comparator: Local infiltration of corticoid crystal suspension into the carpal tunnel without sonographic control

Outcome	Study results and measurements	Absolute effect estimates		Certainty of the Evidence	
Timeframe	study results and measurements	Not sonographic-guided	Sonographic-guided	(Quality of evidence)	
	Relative risk: 0.79	657	519		
Any clinical	(CI 95% 0.34 - 1.81)	per 1000	per 1000	Very low	
improvement	Based on data from 146 participants in 3 studies ¹	Difference: 138 fewer per 1 (CI 95% 434 fewer - 532 mg		Due to very serious inconsistency, Due to serious imprecision ²	
	Relative risk: 1.91	344	657		
Clinical improvement: numbness	(CI 95% 0.25 - 14.78)	per 1000	per 1000	Very low	
	Based on data from 69 participants in 2 studies ³	Difference: 313 more per 1	.000	Due to very serious inconsistency, Due to very serious imprecision ⁴	
		(CI 95% 258 fewer - 4740 m	nore)		
	Relative risk: 0.58	235	136		
Clinical improvement: hand weakness	(CI 95% 0.15 - 2.25)	per 1000	per 1000	Very low	
	Based on data from 39 participants in 1 studies ⁵	Difference: 99 fewer per 10	000	Due to extremely serious imprecision ⁶	
		(CI 95% 200 fewer - 294 mo	ore)		
Clinical improvement:	Relative risk: 0.15	525	79		
non-responder (2 cm	(CI 95% 0.05 - 0.48)	per 1000	per 1000	Low	
or greater on VAS)			1000 wer)	Due to extremely serious imprecision, Upgraded due to Large magnitude of effect ⁸	

Complications: pain Complications: other	Relative risk: 0.66 (CI 95% 0.38 - 1.13) Based on data from 85 participants in 2 studies ⁹ Relative risk: 0.29 (CI 95% 0.17 - 0.49)	450 per 1000 Difference: 153 fewer per 1 (CI 95% 279 fewer - 58 mor 341 per 1000		Moderate Due to serious imprecision ¹⁰ High		
	Based on data from 252 participants in 4 studies ¹¹	Difference: 242 fewer per 1 (CI 95% 283 fewer - 174 fev		12		
Clinical improvement: grip strength	Measured by: Scale: -	Mean	Mean	Moderate		
	Based on data from 190 participants in 3 studies ¹³	Difference: MD 0.57 lower (CI 95% 2.97 lower - 1.82 hi	igher)	Due to serious imprecision ¹⁴		
Pain (VAS)	Measured by: Scale: - Based on data from 165 participants in 3 studies ¹⁵	Mean Difference: SMD 0.49 lower	Mean	High 16		
	Measured by:	(CI 95% 0.80 lower - 0.18 lo	ower)			
BCTQ-SSS	Scale: - Based on data from 439 participants in 8	Mean	Mean	Moderate		
	studies ¹⁷	Difference: SMD 0.79 lower (CI 95% 1.33 lower - 0.26 lo		Due to serious inconsistency ¹⁸		

		Measured by:				
ı	BCTQ-FSS	Scale: -	Mean	Mean	High	
		Based on data from 439 participants in 8 studies ¹⁹	Difference: SMD 0.27 lower (CI 95% 0.46 lower - 0.08 lo		20	
-		Measured by:				
		·	Mean	Mean		
	Time to return to work		Wicum	Wicari		
		21	Difference: null higher			

- 1. Systematic review with included studies: Makhlouf 2014, Omar 2018, Chen 2018 Baseline/comparator Control arm of reference used for intervention.
- 2. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: very serious.** The magnitude of statistical heterogeneity was high, with I^2: 88%., Point estimates vary widely, The direction of the effect is not consistent between the included studies; **Imprecision: serious.** Wide confidence intervals, Low number of patients;
- 3. Systematic review with included studies: Omar 2018, Chen 2018 Baseline/comparator Control arm of reference used for intervention.
- 4. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: very serious.** The magnitude of statistical heterogeneity was high, with I^2: 87%., Point estimates vary widely, The direction of the effect is not consistent between the included studies; **Imprecision: very serious.** Wide confidence intervals, Low number of patients;
- 5. Systematic review with included studies: Chen 2018 Baseline/comparator Control arm of reference used for intervention.
- 6. Imprecision: ~extreme serious. Only data from one study, Low number of patients, Wide confidence intervals;
- $7. \quad \text{Systematic review with included studies: Makhlouf 2014 } \textbf{Baseline/comparator} \ \text{Control arm of reference used for intervention} \ .$
- 8. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; Imprecision: ~extreme serious. Low number of patients, Only data from one study; Upgrade: large magnitude of effect.
- 9. Systematic review with included studies: Chen 2018, Ustun 2013 Baseline/comparator Control arm of reference used for intervention .
- 10. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Imprecision: serious.** Low number of patients;
- 11. Systematic review with included studies: Lee 2014, Roh 2019, Chen 2018, Eslamian 2017 Baseline/comparator Control arm of reference used for intervention.

- 12. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias;
- 13. Systematic review with included studies: Chen 2018, Roh 2019, Rayegani 2019 Baseline/comparator Primary study.
- 14. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious.** Wide confidence intervals;
- 15. Systematic review with included studies: Makhlouf 2014, Chen 2018, Rayegani 2019 Baseline/comparator Control arm of reference used for intervention.
- 16. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
- 17. Systematic review with included studies: Ustun 2013, Roh 2019, Vahdatpour 2019, Chen 2018, Karaahmet 2017, Eslamian 2017, Rayegani 2019, Lee 2014

 Baseline/comparator Control arm of reference used for intervention.
- 18. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 86%., Point estimates vary widely;
- 19. Systematic review with included studies: Chen 2018, Karaahmet 2017, Eslamian 2017, Rayegani 2019, Lee 2014, Ustun 2013, Roh 2019, Vahdatpour 2019

 Baseline/comparator Control arm of reference used for intervention.
- 20. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias;
- 21. Systematic review. Baseline/comparator Control arm of reference used for intervention .

Intervention: Low-level laser therapy for carpal tunnel syndrome

Comparator: Sham therapy

Outcome		Absolute effect estimates		Certainty of the Evidence
Timeframe	Study results and measurements	Sham therapy	Low-level laser therapy for carpal tunnel syndrome	(Quality of evidence)
Pain (dichotomous)	Relative risk: 0.46 (CI 95% 0.33 - 0.62) Based on data from 120 participants in 1 studies ¹	898 per 1000 Difference: 485 f (CI 95% 602 fewe	·	Moderate Due to serious imprecision ²
Clinical improvement: grip strength	Measured by: Scale: - Based on data from 179 participants in 4 studies ³	Mean Difference: SMD (CI 95% 0.05 low	•	Moderate Due to serious inconsistency ⁴
Pain (continuous)	Measured by: Scale: - Based on data from 199 participants in 4 studies ⁵	Mean Difference: SMD (CI 95% 9.64 low		Low Due to serious inconsistency, Due to very serious inconsistency ⁶
BCTQ-SSS	Measured by: Scale: - Based on data from 119 participants in 3 studies ⁷	Mean Difference: MD 9 (CI 95% 14.86 lov	Mean 9.77 lower wer - 4.69 lower)	Low Due to serious risk of bias, Due to serious inconsistency ⁸

BCTA-FSS	Measured by: Scale: -	Mean	Mean	Moderate
	Based on data from 119 participants in 3 studies ⁹	Difference: MD 7.28 lower (CI 95% 10.51 lower - 4.05 lower)		Due to serious risk of bias ¹⁰
Time to return to work		No studies reported this outcome.		
Complications/adverse events		No studies report	ted this outcome.	

- 1. Systematic review with included studies: Lazovic 2014 Baseline/comparator Control arm of reference used for intervention.
- 2. **Imprecision: serious.** Only data from one study, Low number of patients;
- 3. Systematic review with included studies: Tascioglu 2012, Shooshtari 2008, Ekim 2007, Chang 2008 Baseline/comparator Control arm of reference used for intervention.
- 4. **Risk of Bias:** no serious. Inadequate sequence generation/ generation of comparable groups, resulting in potential for selection bias, Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Inconsistency:** serious. The magnitude of statistical heterogeneity was high, with I^2: 59%., Point estimates vary widely; **Imprecision:** no serious. Low number of patients;
- 5. Systematic review with included studies: Ekim 2007, Abid Ali 2012, Tascioglu 2012, Shooshtari 2008 Baseline/comparator Control arm of reference used for intervention.
- 6. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias; **Inconsistency: very serious.** Point estimates vary widely, The magnitude of statistical heterogeneity was high, with I^2: 98%.; **Indirectness: no serious.** The outcome time frame in studies were insufficient;
- 7. Systematic review with included studies: Chang 2008, Abid Ali 2012, Ekim 2007 Baseline/comparator Control arm of reference used for intervention .
- 8. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Inconsistency: serious.** Point estimates vary widely, The confidence interval of some of the studies do not overlap with those of most included studies/ the point estimate of some of the included studies., The magnitude of statistical heterogeneity was high, with I^2: 96%.; **Imprecision: no serious.** Low number of patients;
- 9. Systematic review with included studies: Abid Ali 2012, Ekim 2007, Chang 2008 Baseline/comparator Control arm of reference used for intervention.
- 10. **Risk of Bias: serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Imprecision: no serious.** Low number of patients;

Intervention: Surgical treatment with tourniquet

Comparator: Surgical treatment without tourniquet

Outcome	Absolute effect estimates		Certainty of the Evidence	
Timeframe	measurements	Surgical treatment without tourniquet	Surgical treatment with tourniquet	(Quality of evidence)
Pain (dichotomous: VAS >4)	Relative risk: 4.88 (CI 95% 2.06 - 11.55) Based on data from 85 participants in 1 studies ¹	119 per 1000 Difference: 462 more per 1000 (CI 95% 126 more - 1255 more)	581 per 1000	Moderate Due to serious indirectness, Due to serious imprecision, Upgraded due to Large magnitude of effect ²
Complications/adverse events	Relative risk: 0.99 (CI 95% 0.06 - 16.64) Based on data from 145 participants in 2 studies ³	56 per 1000 Difference: 1 fewer per 1000 (CI 95% 53 fewer - 876 more)	55 per 1000	Very low Due to very serious inconsistency, Due to serious indirectness, Due to serious imprecision, Due to very serious imprecision ⁴
Pain (continous)	Measured by: Scale: - Based on data from 392 participants in 7 studies ⁵	Mean Difference: MD 2.72 higher (CI 95% 2.19 higher - 3.24 higher)		Moderate Due to serious indirectness ⁶
BCTQ-SSS	Measured by: Scale: - Based on data from 151 participants in 2 studies ⁷	Mean Difference: SMD 0.07 higher	Mean	Moderate Due to serious inconsistency ⁸

		(CI 95% 0.56 lower - 0.70 higher)		
BCTQ-FSS	Measured by: Scale: -	Mean	Mean	Moderate
	Based on data from 151 participants in 2 studies ⁹	Difference: SMD 0.36 higher (CI 95% 0.32 lower - 1.05 higher)		Due to serious inconsistency ¹⁰
Time to return to work	Measured by: Scale: - Based on data from 0	Mean	Mean	
	participants in 0 studies ¹¹	Difference: null higher		

- 1. Systematic review with included studies: Farzam 2021 Baseline/comparator Control arm of reference used for intervention.
- 2. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias; **Indirectness: serious.** Differences between the outcomes of interest and those reported (e.g short-term/surrogate,not patient-important), The outcome time frame in studies were insufficient; **Imprecision: serious.** Only data from one study, Low number of patients; **Upgrade: large magnitude of effect.**
- 3. Systematic review with included studies: Okamura 2021, Saleh 2021 Baseline/comparator Control arm of reference used for intervention.
- 4. **Inconsistency: very serious.** Point estimates vary widely, The direction of the effect is not consistent between the included studies, The magnitude of statistical heterogeneity was high, with I^2: 66%.; **Indirectness: serious.** Differences between the outcomes of interest and those reported (e.g short-term/surrogate,not patient-important), The outcome time frame in studies were insufficient, Differences between the outcomes of interest and those reported (e.g short-term/surrogate,not patient-important); **Imprecision: very serious.** Wide confidence intervals, Low number of patients;
- 5. Systematic review with included studies: Gunasagaran 2017, Braithwaite 1993, Lee 2020, Iqbal 2018, Ralte 2010, Okamura 2021, Saleh 2021 Baseline/comparator Control arm of reference used for intervention.
- 6. **Risk of Bias: no serious.** Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Indirectness: serious.** Differences between the outcomes of interest and those reported (e.g short-term/surrogate,not patient-important), The outcome time frame in studies were insufficient;
- 7. Systematic review with included studies: Iqbal 2018, Okamura 2021 Baseline/comparator Control arm of reference used for intervention .
- 8. **Risk of Bias: no serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 74%.;
- 9. Systematic review with included studies: Okamura 2021, Iqbal 2018 Baseline/comparator Control arm of reference used for intervention .

- 10. **Risk of Bias: no serious.** Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias, Selective outcome reporting; **Inconsistency: serious.** The magnitude of statistical heterogeneity was high, with I^2: 78%.;
- 11. Systematic review. **Baseline/comparator** Control arm of reference used for intervention.

Limitations

Comparing the difference from baseline required an ANOVA or ANCOVA analysis, which RevMan does not support. In some of the studies the intervention and control groups were different at baseline, so ideally an ANOVA be a suitable analysis. Because of the limited resources for this clinical practice guidelines, we did not perform such analyses.

We conducted these systematic reviews without having set protocols in the beginning. As a result, we followed the protocols sets in available Cochrane reviews and made pragmatic decisions as we made progress. However, we did not change the set outcomes at the beginning of the project.

Because of limited resources allocated to this project, we only analysed five outcomes. There might be other important outcomes to be considered for the treatment of carpal tunnel syndrome.

We have run double-checking as the good research practice only for 25% of included studies to detect major errors. Although this practice resulted in one sensitivity analysis, we could not find any major errors. However, since 75% percent of the included studies have not been double-checked, there is a possibility of error. Since the final results have been checked by the clinicians and they found the results compatible with the results in clinical practice, we assumed there is no major errors in the remaining studies.

For some of the studies and because of limited time for the evidence synthesis for guideline, we could not access the data from some of the studies; however, we tried to obtain data from Saleh 2021 and extracted more data from the figures to use in the peer-reviewed publications.

Since the primary studies did not report the prevalence of the disease, GRADEpro could not estimate the pre-test probability. This item usually is not being reported as part of GRADE tables.

Direct extraction of TN/FN/TP/FP was not possible via the studies and requires re-calculations; since this was not necessary at this stage, we will consider them for the future publication and present them in 2x2 table.

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