



Effectiveness of surgical versus conservative treatment for carpal tunnel syndrome: A systematic review, meta-analysis and qualitative analysis

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Background: Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper limb. Treatment options include physiotherapy, splinting, steroid injections or surgery.

Objective: To compare the effectiveness of surgical versus conservative treatment for CTS for symptom and functional improvement and improvement of neurophysiological parameters.

Methods: Systematic searches of PubMed and EBSCO host were conducted to identify the studies published between 1990 and 2016, comparing any surgical treatment to any conservative treatment. Participants were adults with a diagnosis of CTS, with symptom duration ranging from 8 months to 3 years. A meta-analysis and a qualitative analysis were conducted to summarize the results of the included studies and establish any agreement between the two.

Results: A total of 15 studies were included in the study and 10 were included in the meta-analysis, involving 1787 wrists. The qualitative and quantitative analyses were consistent with the results of both indicating that surgical treatment leads to a greater improvement of symptoms at six months (mean difference: 0.52, 95%CI 0.27 to 0.78) and a greater improvement of neurophysiological parameters [distal motor latency (mean difference: 0.31, 95%CI 0.06 to 0.56), sensory nerve conduction velocity (mean difference: 3.71 m/s, 95%CI 1.94 to 5.49)]. At 3 months and 12 months, the results were not significant in favor of surgery or conservative treatment.

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Conclusion: Conservative treatment for CTS should be preferred for mild and short-term CTS. Surgery is more effective than conservative in CTS, and should be considered in persisting symptoms, taking into account the complications, which are more severe after surgery. Further research should focus on the field of manual therapy and compare it to surgical treatment for CTS.

Keywords: Carpal tunnel syndrome; median nerve entrapment; surgical treatment; conservative treatment; systematic review; meta-analysis.

Introduction

Carpal tunnel syndrome (CTS) remains more common among non-computer-related jobs,¹ despite the increasing usage of computers in recent years, affecting approximately 1–5% of the general population^{2–4} and approximately 34% of hospital workers.⁵ CTS is a result of compression of the median nerve at the wrist due to the confined space of the carpal tunnel which restricts the movement of the tissues. Any increase in internal or external canal pressure results in neurological impairment with numbness and tingling along the distribution of the nerve. CTS often results from repetitive strain in manual jobs but it is also associated with conditions like rheumatoid arthritis,⁶ pregnancy due to water retention,⁷ and diabetes mellitus, which increases the likelihood of a symptomatic response in an already compressed nerve.⁸ Conservative treatment with physiotherapy, wrist splints, corticosteroid injections, diuretics, vitamin B6 is proposed initially, whereas surgical treatment is reserved for more severe cases with thenar muscle atrophy or after failure of conservative treatment.⁹

Previous systematic reviews have reported an advantage of surgery over conservative treatment for symptom functional improvement.^{10,11} These reviews were published in the last decade. More recent trials have been published since, some of which contradict the results suggested in these reviews. Given a substantial number of recent studies, an updated systematic review is justified to incorporate data brought to light since 2011. Furthermore, this review includes both a meta-analysis and a qualitative analysis to formulate conclusions regarding the relative effectiveness of the interventions.

Therefore, this review sought to investigate whether surgical treatment for CTS can lead to greater symptom improvement, greater functional improvement and greater improvement of neurophysiological

parameters than conservative treatment, both short term (3 months) and long term (12 months). An additional aim was to establish the extent of agreement between a qualitative analysis of the studies and a meta-analysis.

Material and Methods

Identification and selection of literature

Systematic searches of PubMed and EBSCO host were conducted to identify studies written in English and published between 1990 and 2016 (see [Appendix A](#) for full search strategy). Manual searches of reference lists from previous studies were also conducted to ensure that all relevant studies were captured. Studies eligible for inclusion were randomized controlled trials, clinical trials (CTs), prospective and retrospective studies comparing any surgical intervention to any conservative intervention for CTS patients. The outcome measures short-term and long-term improvement of symptoms, functional status and improvement of neurophysiological parameters. Case control studies were excluded. Studies comparing surgical interventions and studies comparing conservative interventions were also excluded as the aim was to compare the relative effectiveness of the two interventions.

Two independent investigators (KD and MI) screened the titles and read the abstracts and the relevant papers were obtained in full text to assess further eligibility. Data extraction was performed by the two investigators independently. The following data were extracted: authors, year of publication, study design, description of the sample, description of the surgical and conservative intervention, duration of study, study outcomes, assessment times, study results and study conclusions.

Quality assessment

The methodological quality of the randomized controlled trials and CTs included in this systematic review were assessed using the CBRG methodological criteria scale proposed by van Tulder *et al.*¹² This scale consists of 11 items and is similar to the PEDro scale, which has good levels of validity and reliability,^{13,14} but with clearer operationalization criteria. It addresses the internal validity of the studies in order to minimize the risk of systematic bias (selection bias, performance bias, attrition bias and performance bias). Items relate to the adequacy of the randomization, treatment allocation concealment, baseline similarity of treatment groups, patient, treatment provider and assessor blinding, similarity of co-interventions, adequacy of compliance, adequacy and description of the dropout rate, similar assessment timing across groups and analysis according to intention-to-treat. Each item is accompanied by a strict list and was evaluated with a “yes”, “no”, or “unclear” (if it did not apply or if it was not mentioned). Each positive answer scored 1 point. The studies were regarded as high quality if the total score of positive answers in the criteria list was seven and above. In consequence, if the total score was below seven, studies were regarded as low quality.

The methodological quality of the prospective and retrospective studies was assessed using the methodological criteria scale proposed by Moga *et al.*¹⁵ using a modified Delphi technique. This scale is made up of 18 items addressing methodological quality (i.e., patient characteristics, adequacy of eligibility criteria, adequacy of intervention, similarity of co-interventions, relevance and timing of outcome measures) and statistical reporting (i.e., suitability of statistical tests, length and loss of follow-up, random variability, adverse effect and competing interest reporting). Each item was accompanied by a strict list and was evaluated with a “yes” or “no” and each positive answer scored 1 point. The studies were regarded as high quality if the total score of positive answers was 14 and above. If the total score was below 14, then the studies were regarded as low quality. The methodological quality result was used for the formulation of conclusions in the qualitative analysis, which is described further below.

Participants

Studies involving patients diagnosed with CTS irrespective of the cause, the way it was diagnosed, other associated conditions, the age or the sex of the person. Patient characteristics such as age, sex, duration of symptoms were recorded in order to assess heterogeneity between studies.

Intervention

The included studies compared any surgical intervention such as open carpal tunnel release (OCTR) or endoscopic carpal tunnel release (ECTR) to any conservative intervention such as steroid injections, wrist splints, physiotherapy with electrotherapy, exercise or manual therapy or a combination of different modalities.

Outcome measures

The primary outcome was the patient self-reported improvement in symptoms and function measured using the symptom severity scale and functional status scale of the Boston questionnaire (BQ). Secondary outcome measures used to evaluate the effectiveness of the intervention were improvement of neurophysiological parameters measured using electrodiagnostic studies, and side effects reported.

Data analysis

Data extraction was performed by one investigator (KD) and cross-checked by another (MI). Data were documented on a customized table in order to compare patient demographics, parameters of intervention, duration and outcome measures of each study post-intervention. Where sufficient information was obtainable and the outcome measures were comparable, meta-analyses were performed, allowing a quantitative analysis of the studies. The pooled estimations regarding outcomes were expressed as dichotomous or as continuous variables. These were calculated using a random effect model or a fixed effect model. For dichotomous data, the pooled odds ratio (OR) was calculated. The pooled mean difference was estimated to assess continuous data. Statistical analyses were performed using the Review Manager (RevMan) Version 5.0 software (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen,

Denmark, 2008) and STATA Version 13. $P < 0.05$ was considered significant.

Heterogeneity analysis

The existence of statistical heterogeneity between the included studies was assessed using the I^2 test. The heterogeneity was considered low, moderate or high if the I^2 was 25%, 50% or $> 75\%$, respectively.¹⁶ If p -value was less than 0.05, the random effect model was adopted or vice versa. The between-trial heterogeneity was assessed using the Q test and the I^2 statistic.¹⁷ Subgroup analyses by month were conducted in order to explore potential sources of the between-trial heterogeneity and potential effect modifiers in this study.

Publication bias assessment

To assess asymmetry, funnel plots were formulated. The Begg's rank correlation and Egger's linear regression tests were used to detect potential publication bias.¹⁸ A two-tailed p -value < 0.10 for Egger regression indicated the presence of publication bias.

Sensitivity analyses

The influence of individual studies, from which the meta-analysis estimates are derived, was examined by omitting low quality studies to see the extent to which inferences depend on a particular study or group of studies (sensitivity analysis).

Qualitative analysis

Based on the methodological quality score of each study, a qualitative analysis was also performed to formulate conclusions thus allowing a wider inclusion of studies. This was done using the Best Evidence Synthesis,¹² which was modified to include observational studies. This method consists of five levels of scientific evidence, presented in **Box 1**. Consistency was defined *a priori* at 60% (i.e., if 60% or more of studies agreed in the same direction of results).

Results

Selection of studies

From the search strategy, 459 potentially relevant studies were identified and 252 duplicate paper were removed after checking titles and abstracts. Out of these studies, 15 fulfilled the inclusion

Box 1. Synthesis of results for the qualitative analysis.

Strong	Consistent findings among two or more, high quality RCTs
Moderate	Consistent findings among one high quality RCT and one or more low quality RCTs and/or CTs or one high quality observational study
Limited	Consistent findings from one high quality RCT, or one low quality RCT or CT, or one high quality observational study
Conflicting	Inconsistent findings among multiple studies (RCTs, CTs and/or observational studies)
No evidence from studies	No studies found

criteria and were eligible for data analysis. Of these, nine were Randomized CTs (RCTs), two were CTs, two were prospective studies and two were retrospective studies. The meta-analysis only included 10^{17–26} of these studies with similar outcome measures, whereas all the studies were included in the qualitative analysis. The flow of studies through the selection process is presented in **Fig. 1**. (see **Appendix B** for excluded papers). A summary of the studies is presented in **Table 1**.

Study characteristics

Quality

The methodological quality of the eligible studies was low to moderate. There was a mean CBRG score of 5.1 out of 11 for the 9 RCTs and the 2 CTs. CTs had a lower quality score (2/11) due to lack of randomization, whereas the maximum score in RCTs was 8/11. Due to the nature of the intervention (surgery), neither the patient nor the therapist could be blinded (criteria 4 and 5), so the highest score that could be expected was 9/11. Only 4 out of 11 trials had 80% retention rates for short-term follow-up and 70% for long-term follow-up and compliance was not clearly stated in the studies with the exception of one.²⁷ There was a mean score of 13 out of 18 of the criteria proposed by Moga *et al.*¹⁵ for 2 prospective and the 2 retrospective studies (range 11 to 17). Quality scores are presented in **Tables 2** and **3**.

Participants

The review included 1787 wrists with a clinical diagnosis of CTS. The sample sizes of the 15 eligible

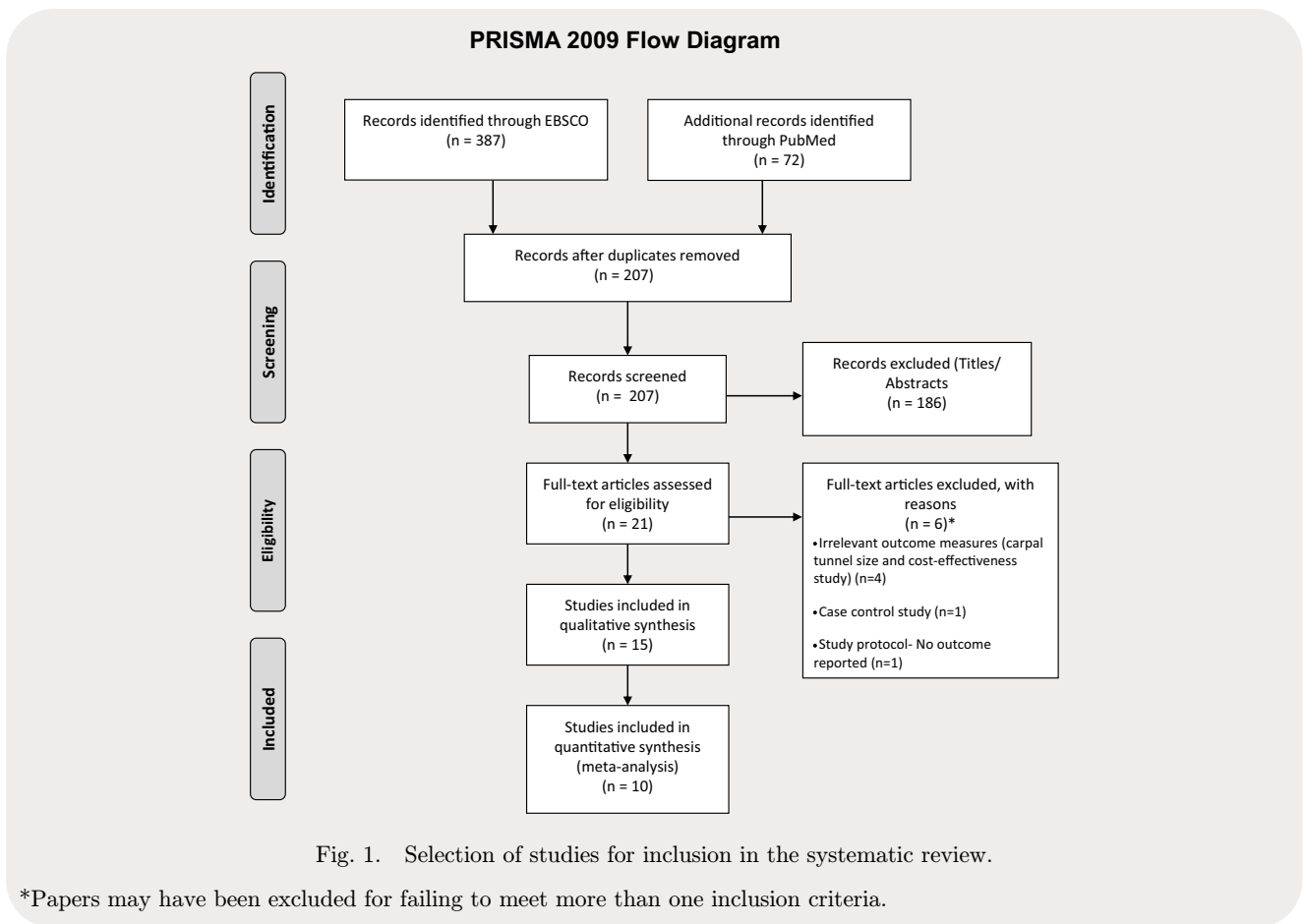


Fig. 1. Selection of studies for inclusion in the systematic review.

studies ranged from 40 to 429 participants. Participants were mostly females (79%) and one study²⁸ included only women. The weighted mean age in the studies included was 48.8 years ranging from 20 years old¹⁹ to 88.5 years old²⁹ although one study concerned an elderly population,²⁹ affecting the overall mean age. The duration of symptoms ranged from 8 months²⁰ to 3 years.²⁷

Intervention

All eligible studies compared surgery (OCTR or ECTR) to a conservative intervention. Conservative interventions involved the use of steroid injections in six studies,^{20–25} splinting in two studies,^{22,26} Low Level Laser Therapy (LLLT) in one study,³⁰ manual physical therapy in one study²⁸ and multimodality in four studies.^{19,27,29,31} The treatment period in the CTs ranged from a single application to three months.

Outcome measures

Symptom severity and functional status were assessed using the BQ in six studies,^{22,23,26,28,29}

which comprises of the Symptom Severity Scale (11 items) and the Functional Status Scale (8 items). The BQ is a self-administered CTS-specific tool measuring symptom severity and functional status on a scale of 1 to 5, where 1 = no symptoms or no difficulty and 5 = very severe symptoms or so difficult and could not do activity) and the overall score is the mean of all items out of 5. High scores are indicative of more severe symptoms or functional limitation. The BQ's validity and reliability have been previously assessed.³² One study²⁷ used the CTS assessment questionnaire (CTSAQ) to assess the symptoms (11 item scale) and functional status (9 item scale) on a 1–5 scale similar to the BQ. Symptom severity was assessed with the Global symptom score (GSS) in two studies.^{24,25} This scoring system rates symptoms on a scale of 0 (no symptoms) to 10 (severe) in five categories: pain, numbness, paresthesia, weakness/clumsiness and nocturnal awakening, and the result is the sum of the scores out of 50. Three publications of the same study^{20,33,34} assessed the functional status on a 100 mm Visual Analogue Scale (VAS), where 0 = no functional impairment and 100 = the most

Table 1. Characteristics of included studies ($n = 15$).

Study	Design	Participants	Intervention	Outcome measures
Ref. 19	Retrospective	Incl = Clinical diagnosis of CTS confirmed by EDS $n = 265$ patients Sex = 43%F/57%M (114F/151M) Age [μ (range)] = 45 (20–90) yrs; Gp A: 49 yrs; Gp B: 42 yrs	A = OCTR or ECTR (95 wrists/77 patients) B = Multimodality (patient education, wrist splinting, vitamin B, NSAIDs, steroid injections and job change or modification) (188 patients) All groups = educational videotape and brochure, wrist splints, 100 mg Vit B6 and 50 mg B2 daily and NSAIDs.	<ul style="list-style-type: none"> • Patient satisfaction = Subjective • Repeat history, physical examination and nerve conduction studies = Objective findings • Follow-up = 3 to 9 month intervals (for group B)
Ref. 21	Prospective	Incl = Clinical diagnosis of CTS confirmed by EDS $n = 125$ wrists Sex = Gp A: 76%F/24%M; Gp B: 81%F/19%M; Gp C: 79%F/21%M Age [median (range)] = Gp A: 57.5 (30–88) yrs; Gp B: 58.6 (28–87) yrs; Gp C: 57.6 (28–87) yrs Symptom duration (μ) = Gp A: 23.3 mo; Gp B: 22.9 mo; Gp C: 20.9 mo	A = OCTR or ECTR (33 wrists) B = 1–3 doses steroid injections (56 wrists) C = No local treatment. NSAIDs or vascular drugs (36 wrists)	<ul style="list-style-type: none"> • Improvement of neurophysiological parameters for median nerve: SNCV • Follow-up = Month: 1, 6 and 12
Ref. 31	Prospective	Incl = Clinical diagnosis of CTS > 1 mo $n = 429$ patients Sex = Gp A: 191F/79M; Gp B: 102F/23M Age ($\mu \pm$ SD) = (3 subgroups) ($\mu \pm$ SD): A1: 68.0 \pm 9.1 yrs; A2: 42.0 \pm 7.3 yrs; A3: 39.0 \pm 8.1 yrs; B1: 64.0 \pm 7.0 yrs; B2: 41.0 \pm 8.9 yrs; B3: 37.0 \pm 8.8 yrs	A1, A2 and A3 = OCTR or ECTR (270 patients) B1, B2 and B3 = Multimodality (125 patients) [NSAIDs (96), wrist splints (115), physiotherapy (42), work modification (70), steroid injections (48), Vitamin B6 (13)]	<ul style="list-style-type: none"> • Symptoms = SSS — 11 items (5-point scale) • Function = FSS — 8 items (5-point scale) • Satisfaction = satisfaction scale 7 items (5-point scale) • Health status = SF-36: 36 questions assessing general health-related quality of life • Follow-up = Month: 6, 18 and 30
Ref. 23	CT	Incl = Clinical diagnosis of unilateral CTS > 6 mo, confirmed by EDS $n = 90$ patients Sex = Gp A: 38F/6M; Gp B: 42F/4M Age ($\mu \pm$ SD) = Gp A: 48.0 \pm 8.4 yrs; Gp B: 45.3 \pm 9.9 yrs	A = OCTR (44 patients) B = 2 doses steroid injections 2 wks apart of 6.4 mg betamethasone (46 patients) 23-gauge needle at anterior wrist flexion crease, angulation 45° distally and 45° radially	<ul style="list-style-type: none"> • Symptoms = BQ — 11 items (5-point scale) • Function = BQ — 8 items (5-point scale) • Improvement of neurophysiological parameters for median and ulnar nerves = DML, MNCV, CMAP, DSL, SNCV, SNAP using the Nihon Kohden-Neuropack MEB 5504 K • Follow-up = Month: 3 and 6

Table 1. (Continued)

Study	Design	Participants	Intervention	Outcome measures
Ref. 26	RCT	Incl = Pain or paraesthesiae in the median nerve distribution, clinical diagnosis of CTS, confirmed by EDS, age > 18 yrs, ability to fill out questionnaires in Dutch <i>n</i> = 176 Sex = Gp A: 66F/11M; Gp B: 77F/2M Age ($\mu \pm SD$) = Gp A: 49 \pm 11; Gp B: 49 \pm 12 Symptom Duration [median (IQR)] = Gp A: 40 (16–104) wks; Gp B: 52 (24–104) wks Characteristics = small heterogeneity in sex and symptom duration	A = OCTR (87) B = Splinting in neutral position of wrist for 6 wks min at night and during the day as preferred (89)	<ul style="list-style-type: none"> • General improvement = 6-point ordinal transition scale (success = “completely recovered” or “much improved”) • No. of nights the patient woke due to symptoms in the last week • Symptoms = 11-point scale • Symptoms = SSS — 11 items (5-point scale) • Function = FSS — 8 items (5-point scale) • Severity of CTS-related complaints-Physiotherapist assessment on 11-point scale • Improvement of neurophysiological parameters for median nerve = DML, DSL, Median-Ulnar DSL difference • Follow-up = Month: 3, 6 and 12
Ref. 24	RCT	Incl = Clinical diagnosis of CTS > 3 mo but < 1 yr confirmed by EDS <i>n</i> = 50 patients Sex = 48F/2M; Gp A: 24F/1M; Gp B: 24F/1M Age ($\mu \pm SD$) = Gp A: 50.8 \pm 11.6 yrs; Gp B: 48.2 \pm 6.5 yrs Characteristics = no large heterogeneity in age, symptom severity, baseline measurements	A = OCTR (25 patients) B = 1 dose steroid injection 15 mg methylprednisolone acetate with 25-gauge needle 30° angle medial to Palmaris longus tendon (25 patients)	<ul style="list-style-type: none"> • Symptoms = GSS — 11-point scale for five symptom categories, total score/50 • Improvement of neurophysiological parameters for median nerve = DML, SNCV • Grip strength = JAMAR hydraulic hand dynamometer • Follow-up = week: 6 and 20
Ref. 20	RCT	Incl = Age \geq 18 yrs, Clinical diagnosis of CTS > 3 mo, confirmed by EDS, consecutive referral and unresponsiveness to \geq 2 wks NSAIDs treatment <i>n</i> = 163 wrists/101 patients Sex: 93F/8M Age ($\mu \pm SD$) = Gp A: 50.53 \pm 10.87 yrs; Gp B: 53.17 \pm 13.93 yrs (<i>p</i> = 0.213) Symptom duration ($\mu \pm SD$): Gp A: 31.12 \pm 7.27 wks; Gp B: 33.25 \pm 8.17 wks (<i>p</i> = 0.723)	A = OCTR (80 wrists) B = 1 or 2 doses steroid injection 20 mg in 1 mL paramethasone acetamide with 22-gauge needle 45° angle distally 1–2 cm depth medial to Palmaris longus tendon (83 wrists)	<ul style="list-style-type: none"> • Nocturnal paresthesias = 100 mm VAS • Diurnal pain = 100 mm VAS • Functional impairment = 100 mm VAS • Follow-up = month: 3, 6 and 12

Table 1. (Continued)

Study	Design	Participants	Intervention	Outcome measures
Ref. 29	Retrospective	Incl = Age ≥ 70 yrs, Recent clinical diagnosis of CTS, with or without normal EDS, county residents $n = 96$ wrists/60 patients Sex = 43F/27M Age [μ (range)]: 77.0 (70.2–88.5) yrs Characteristics = no large heterogeneity in age, symptom duration or symptom severity	A = OCTR or ECTR (47 wrists) B = Multimodality (NSAIDs, splinting, steroid injections) (41 wrists)	<ul style="list-style-type: none"> • Symptoms = BQ — 11 items (5-point scale) • Function = BQ — 8 items (5-point scale) • Patient expectations and satisfaction = MODEMSQ — Musculoskeletal Outcome Data Evaluation and Management System Questionnaire — 5 items • Health status = SF-36: 36 questions assessing general health-related quality of life • Follow-up = N/A
Ref. 22	RCT	Incl = Clinical diagnosis of mild to moderate CTS > 6 mo confirmed by EDS $n = 57$ wrists Sex = 53F/4M Age ($\mu \pm SD$) = Gp A: 45.27 \pm 13.19 yrs; Gp B: 44.50 \pm 7.24 yrs; Gp C: 44.46 \pm 8.52 yrs ($p = 0.976$) Symptom duration ($\mu \pm SD$): Gp A: 21 \pm 11 mo; Gp B: 15.26 \pm 7.19 mo; Gp C: 19.13 \pm 13 mo ($p = 0.869$)	A = OCTR (11) B = Splinting (23) in neutral position of the wrist for 3 mo night and day C = Splinting & 1 dose steroid injection (23)	<ul style="list-style-type: none"> • Improvement of neurophysiological parameters for median nerve = DML, PML, MNCV, CMAP wrist and elbow, SNCV, SNAP using the Nihon-Cohden Neuropack • Symptoms = BQ — 11 items (5-point scale) • Function = BQ — 8 items (5-point scale) • Satisfaction = 5-point scale • Follow-up = month: 3 and 6
Ref. 30	CT	Incl = Clinical diagnosis of CTS $n = 60$ wrists/54 patients Sex = Gp A: 23F/4M; Gp B: 25F/2M Age ($\mu \pm SD$) = Gp A: 42.65 \pm 8.0 yrs; Gp B: 49.11 \pm 7.23 yrs Symptom duration ($\mu \pm SD$) = Gp A: 36.17 \pm 4.38 mo; Gp B: 28.21 \pm 7.03 mo	A = OCTR (30 wrists) B = LLLT Neon (He-Ne) (632.8 nm, Level Laser M300) continuous wave (CW), ≥ 12 mW, 30 cm from skin, 3 J/cm ² , 2x/wk for 12 sessions (30 wrists)	<ul style="list-style-type: none"> • % patients with • Symptom relief • Return to normal activities • Adverse effects from treatment • Positive nerve conduction tests • Follow-up = month: approximately 6

Table 1. (Continued)

Study	Design	Participants	Intervention	Outcome measures
Ref. 27	RCT	Incl = Age \geq 18 yrs, Clinical diagnosis of CTS > 2 wks confirmed by EDS, +ve "flick test" or nocturnal pain, failure of 2 wks conservative treatment $n = 116$ patients Sex = Gp A: 28F/29M; Gp B: 34F/25M Age ($\mu \pm$ SD) = Gp A: 50.2 \pm 10.3 yrs; Gp B: 51.2 \pm 8.9 yrs ($p = 0.213$) Symptom duration [median (IQR)] = Gp A: 3.2 (1.3–5.5) yrs; Gp B: 3.4 (1.0–8.7) yrs	A = OCTR or ECTR (57 patients) B = Multimodality [200 mg ibuprofen 3x/day, 6 sessions hand therapy over 6 wks, educational booklet, hand exercises, splinting night and day, work modifications] (59 patients)	<ul style="list-style-type: none"> • Function = CTSAQ — 9 items (5-point scale) • Symptoms = CTSAQ — 11-items (5-point scale) • Pain interference with work or activities = 11-point scale • Health status = SF-36: 36 questions assessing general health-related quality of life • Additional treatments = Patient diary • Follow-up = month: 6 and 12
Ref. 33	RCT	Incl = Age \geq 18 yrs, Clinical diagnosis of CTS > 3 mo, confirmed by EDS, consecutive referral and unresponsiveness to \geq 2 wks NSAIDs treatment $n = 163$ wrists/101 patients Sex: 93F/8M Age ($\mu \pm$ SD) = Gp A: 50.53 \pm 10.87 yrs; Gp B: 53.17 \pm 13.93 yrs ($p = 0.213$) Symptom duration ($\mu \pm$ SD): Gp A: 31.12 \pm 7.27 wks; Gp B: 33.25 \pm 8.17 wks ($p = 0.723$)	A = OCTR (80 wrists) B = 1 or 2 doses steroid injection 20 mg in 1 mL paramethasone acetone with 22-gauge needle 45° angle distally 1–2 cm depth medial to Palmaris longus tendon (83 wrists)	<ul style="list-style-type: none"> • Nocturnal paresthesias = 100 mm VAS • Diurnal pain = 100 mm VAS • Functional impairment = 100 mm VAS • Follow-up = month: 3, 6, 12 and 24
Ref. 34	RCT	Incl = Age \geq 18 yrs, Clinical diagnosis of CTS > 3 mo, confirmed by EDS, consecutive referral and unresponsiveness to \geq 2 wks NSAIDs treatment $n = 163$ wrists/101 patients Sex: 93F/8M Age ($\mu \pm$ SD) = Gp A: 50.53 \pm 10.87 yrs; Gp B: 53.17 \pm 13.93 yrs ($p = 0.213$) Symptom duration ($\mu \pm$ SD): Gp A: 31.12 \pm 7.27 wks; Gp B: 33.25 \pm 8.17 wks ($p = 0.723$)	A = OCTR (80 wrists) B = 1 or 2 doses steroid injection 20 mg in 1 mL paramethasone acetone with 22-gauge needle 45° angle distally 1–2 cm depth medial to Palmaris longus tendon (83 wrists)	<ul style="list-style-type: none"> • Nocturnal paresthesias = 100 mm VAS • Diurnal pain = 100 mm VAS • Functional impairment = 100 mm VAS • Follow-up = month: 3, 6 and 12 • Improvement of neurophysiological parameters for median nerve = DML, MA, SNCV, SA • Follow-up = month: 12

Table 1. (Continued)

Study	Design	Participants	Intervention	Outcome measures
Ref. 25	RCT	Incl = Clinical diagnosis of CTS confirmed by EDS, symptoms for > 3 mo n = 40 patients Sex = 29F/11M ($p = 0.723$) Age ($\mu \pm SD$) = Gp A: 43.8 \pm 10.98 yrs; Gp B: 46.9 \pm 12.33 yrs ($p = 0.406$) Symptom duration ($\mu \pm SD$) = Gp A: 12.5 \pm 8.76 mo; Gp B: 10.15 \pm 6.75 mo ($p = 0.348$)	A = OCTR (20 patients) B = Steroid injection with 40 mg of methylprednisolone (20 patients)	<ul style="list-style-type: none"> • Symptoms = GSS — 11-point scale for five symptom categories, total score/50 • Follow-up = week: 2, 4 and 12
Ref. 28	RT	Incl = Clinical diagnosis of CTS confirmed by EDS (sensory and motor deficit), symptoms for > 12 mo n = 120 patients Sex = 120F/0M Age ($\mu \pm SD$) = Gp A: 46 \pm 9 yrs; Gp B: 47 \pm 10 yrs Symptom duration ($\mu \pm SD$) = Gp A: 3.5 \pm 3.1 yrs; Gp B: 3.1 \pm 2.7 yrs	A = OCTR or ECTR (60 patients) B = Manual therapy 3 sessions of 30' 1x/wk (60 patients)	<ul style="list-style-type: none"> • Pain intensity = NPRS — 0–10 (11-point scale where 0 = no pain and 10 = worst possible pain) • Symptoms = BQ — 11 items (5-point scale) • Function = BQ — 8 items (5-point scale) • Self-Perceived improvement = GROOC (from -7 (worse) to +7 (better)) • Follow-up = Month: 1, 3, 6 and 12

Notes: Incl = inclusion criteria, n = number of patients randomized, Gp = group, EDS = electrodiagnostic studies, OCTR = Open carpal tunnel release, ECTR = Endoscopic carpal tunnel release, BQ = Boston Questionnaire, SF-36 = Short Form 36, DML = Distal Motor Latency, MNCV = Motor Nerve Conduction Velocity, CMAP = Compound Muscle Action Potential, DSL = Distal Sensory Latency, SNCV = Sensory Nerve Conduction Velocity, SNAP = Sensory Nerve Action Potential, SSS = Symptom severity scale, FSS = Functional status scale, GSS = Global symptom score, VAS = Visual analogue scale, MODEMSQ = Musculoskeletal Outcome Data Evaluation and Management System Questionnaire, PML = Proximal motor latency, C TSAQ = Carpal tunnel syndrome assessment questionnaire, MA = Motor amplitude, SA = Sensory amplitude, RCT = Randomized controlled trial, CT = Clinical trial, RT = Randomized trial, NPRS = Numerical Pain Rating Scale, GROOC = Global rating of change.

Table 2. Quality scores for CTs ($n = 11$).

Study	Randomization adequacy	Allocation concealment	Baseline comparability	Participant blinding	Therapist blinding	Assessor blinding	Cointervention avoidance	Compliance	Dropout rate < 20%	Timing	Intention to treat analysis	Total (0 to 11)
Ref. 23	N	N	Y	N	N	N	U	U	N	Y	N	2
Ref. 26	Y	Y	Y	N	N	Y	Y	N	N	Y	Y	7
Ref. 24	Y	Y	Y	N	N	Y	U	U	Y	Y	N	7
Ref. 20	Y	Y	Y	N	N	N	U	U	Y	Y	Y	6
Ref. 22	Y	U	Y	N	N	N	U	U	U	Y	N	3
Ref. 30	N	N	Y	N	N	N	N	U	U	Y	N	2
Ref. 27	Y	Y	Y	N	N	Y	U	Y	N	Y	Y	7
Ref. 33	Y	Y	Y	N	N	N	U	U	N	Y	Y	5
Ref. 34	Y	Y	Y	N	N	N	U	U	N	Y	N	4
Ref. 25	Y	Y	Y	N	N	U	N	U	Y	Y	N	5
Ref. 28	Y	Y	Y	N	N	Y	Y	U	Y	Y	Y	8

Table 3. Quality scores for prospective and retrospective studies ($n = 4$).

Study	Hypothesis stated	Description of characteristics	Multicenter study	Appropriate eligibility criteria	Consecutive recruitment	Similar stage of condition	Clearly described intervention	Clearly described interventions	Outcome measure description	Outcome measure suitability	Outcome measure timing	Statistical test suitability	Length of follow-up	Loss to follow-up	Random variability	Adverse events	Conclusion supported by result	Competing Interest	Total (0 to 18)
Ref. 19	Y	Y	N	Y	N	N	Y	Y	Y	N	Y	N	Y	N	N	Y	Y	Y	11
Ref. 21	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	Y	N	11
Ref. 31	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	17
Ref. 29	Y	Y	N	Y	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	N	13

severe functional impairment. For meta-analysis purposes, the GSS scores and the VAS scale scores were divided by 10 and 20, respectively, coming up with a common denominator of 5, in order to be coherent with the BQ and CTSAQ scores. The improvement of neurophysiological parameters was carried out by physicians and neurologists with nerve conduction studies. The most commonly assessed parameters were the Distal Motor Latency (DML) and the Sensory Nerve Conduction Velocity (SNCV).

Effect of intervention on symptom improvement

The meta-analysis pooled data from 6 studies with a total of 805 wrists. One study²⁶ was not included in the pooled analysis as it presented the standardized mean difference in contrast to the other studies, which presented the mean score and standard deviation (SD). The results demonstrate that surgical treatment leads to a greater symptom improvement at six months by 0.52 points lower score on a 5-point symptom severity scale compared to conservative treatment 95%CI (0.27 to 0.78). There was a statistically significant high heterogeneity ($I^2 = 82\%$, $p < 0.0001$) (Fig. 2). The results remain similar, if only high quality studies^{17,18,22,26} were included in the meta-analysis

(MD 0.56, 95%CI 0.16 to 0.96, $I^2 = 89\%$, $p < 0.00001$) (see Fig. C.1 in Appendix C). Meta-analysis results at three months further increased the total heterogeneity, therefore it was not astute to present them. Results for 18 or > 18 months could not be calculated due to insufficient data from the included studies.

The qualitative analysis agreed with the meta-analysis, with strong evidence in favor of surgery for symptom improvement at 6 months, conflicting evidence at 12 months, moderate evidence at 18 months and limited evidence for the time period longer than 18 months (Table 4, see also Tables C.1–C.5 in Appendix C for details of included studies).

Effect of intervention on functional improvement

The total meta-analysis results pooled data from 6 studies with a total of 918 wrists. One study²⁶ was not included in the pooled analysis for reasons explained previously. The results demonstrate that surgery was superior to conservative treatment for functional improvement but the result was not significant (MD 0.06, 95%CI -0.10 to 0.22, $I^2 = 84\%$, $p < 0.00001$). Due to the high heterogeneity, a subgroup analysis was fitting. At 3 months and 12 months, there was no statistically

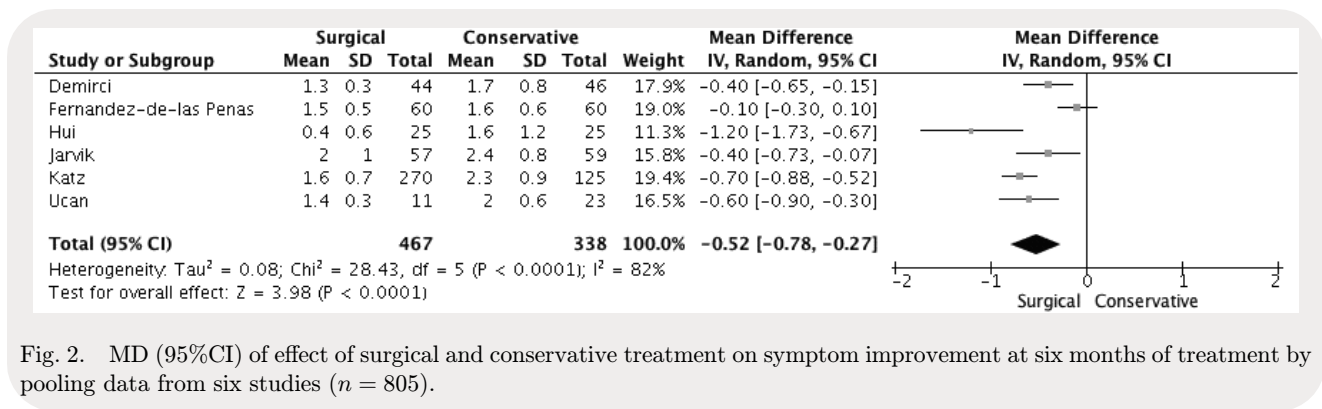


Fig. 2. MD (95%CI) of effect of surgical and conservative treatment on symptom improvement at six months of treatment by pooling data from six studies (n = 805).

Table 4. Qualitative analysis for symptom improvement.

	3 months	6 months	12 months	18 months	> 18 months
Symptom improvement	Conflicting evidence (6 studies)	Strong evidence fav. Surg (8 studies)	Conflicting evidence (4 studies)	Moderate evidence fav. Surg (2 studies)	Limited evidence fav. Surg (2 studies)

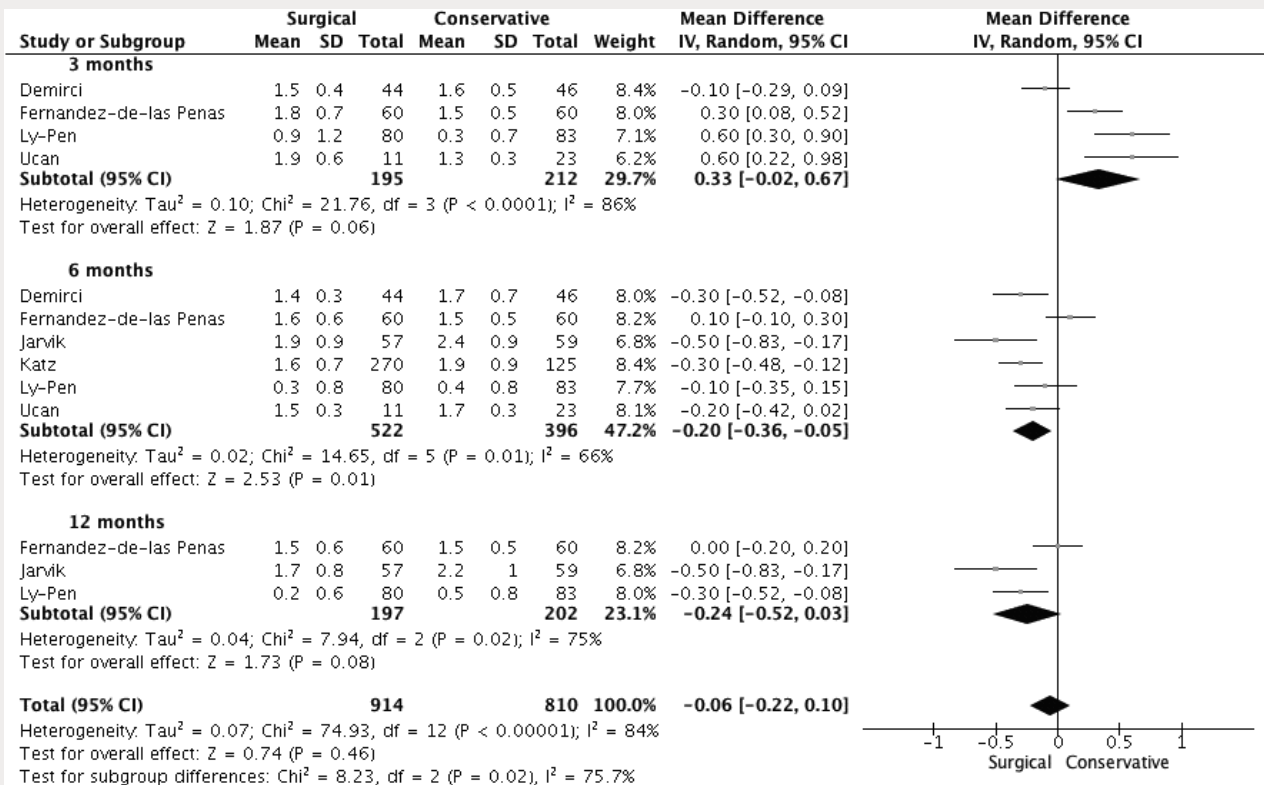


Fig. 3. MD (95%CI) of effect of surgical and conservative treatment on functional improvement at 3, 6 and 12 months of treatment by pooling data from six studies ($n = 918$).

significant difference between the surgical and conservative treatment for function. Surgery proved more effective than conservative treatment at six months (MD 0.20, 95%CI 0.05 to 0.36, $I^2 = 66%$, $p = 0.01$) (Fig. 3, but if only high quality studies^{17,18,26} were included, the results were not statistically significant at six months (MD -0.22, 95%CI -0.55 to 0.12, $I^2 = 85%$, $p = 0.001$). The results remain similar at 12 months (MD -0.23, 95%CI -0.72 to 0.26, $I^2 = 85%$, $p = 0.01$) with data from two studies^{17,18} (see Fig. C.2 in Appendix C).

The qualitative analysis favored surgery with strong evidence at 6 and 12 months and limited evidence for the time period longer than 18 months

(Table 5, see also Tables C.6–C.10 in Appendix C for details of included studies).

Effect of intervention on improvement of neurophysiological parameters

The included studies presented results for different neurophysiological parameters. The meta-analysis was only applicable for the DML and SNCV. Studies assessed the outcomes for the DML between 5 and 12 months. One study²⁴ performed the follow-up measurement at 5 months, another³⁴ at 12 months and two more studies performed the

Table 5. Qualitative analysis for functional improvement.

	3 months	6 months	12 months	18 months	> 18 months
Functional improvement	Moderate evidence fav. Conserv. (5 studies)	Strong evidence fav. Surg. (8 studies)	Strong evidence fav. Surg. (4 studies)	Conflicting evidence (2 studies)	Limited evidence fav. Surg. (2 studies)

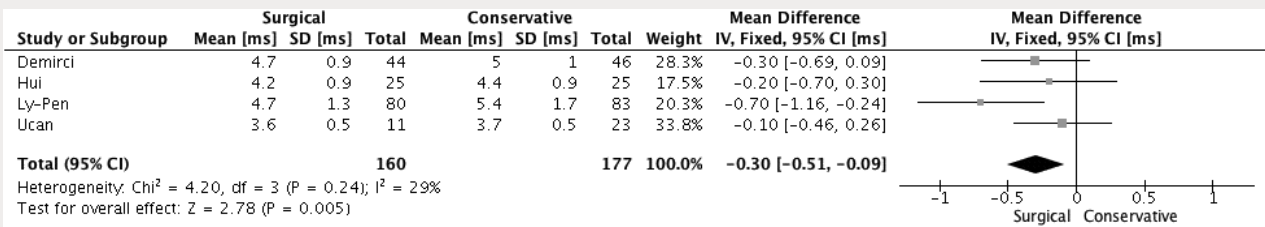


Fig. 4. MD (95%CI) of effect of surgical and conservative treatment on improvement of DML between 5 and 12 months of treatment by pooling data from four studies ($n = 337$).

follow-up at 6 months.^{22,23} Pooled data utilizing 337 wrists demonstrated that surgery provides a greater improvement of the DML compared to conservative treatment with a mean difference 0.30 ms less time delay in the surgical group compared to the conservative (95%CI 0.09 to 0.51) and low to moderate non-significant heterogeneity ($I^2 = 29\%$, $p = 0.24$) (Fig. 4).

In the total meta-analysis results for the SNCV were in favor of surgery (MD 2.73 m/s, 95%CI 0.71 to 4.75) with a total of 80 wrists for the surgical and 94 for the conservative group. There was a moderate non-significant heterogeneity of 52%

($p = 0.08$), which was affected by the results at 3 months, so a subgroup analysis was appropriate (Fig. 5). At 6 months, the results were in favor of surgery (MD 3.71 m/s, 95%CI 1.94 to 5.49, $I^2 = 0\%$, $p = 0.42$).

In contrast to the meta-analysis, the qualitative analysis took into consideration the overall effectiveness from the nerve conduction studies reported in the included studies. The data synthesis demonstrated that there was a benefit in favor of surgery with moderate evidence at 6 and 12 months and insufficient data to formulate conclusions for the long-term effectiveness (Table 6, see

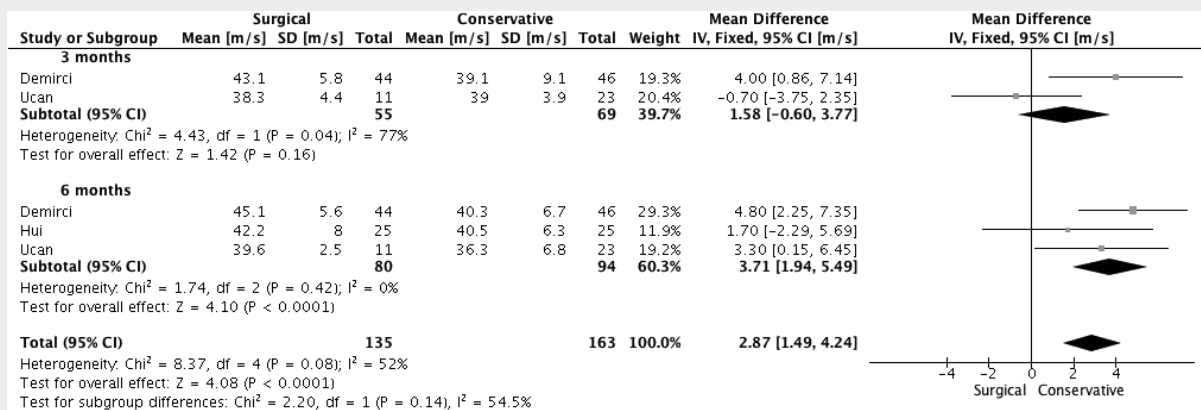


Fig. 5. MD (95%CI) of effect of surgical and conservative treatment on improvement of SNCV at six months of treatment by pooling data from three studies ($n = 174$).

*Left = results in favor of surgery, Right = results in favor of conservative treatment.

Table 6. Qualitative analysis for improvement of neurophysiological parameters.

	3 months	6 months	12 months	18 months	> 18 months
Improvement of neurophysiological parameters	Conflicting evidence (2 studies)	Moderate evidence fav. Surg (3 studies) Limited evidence fav Surg. for DML (1 study)	Moderate evidence fav. Surg (3 studies)	N/A	N/A

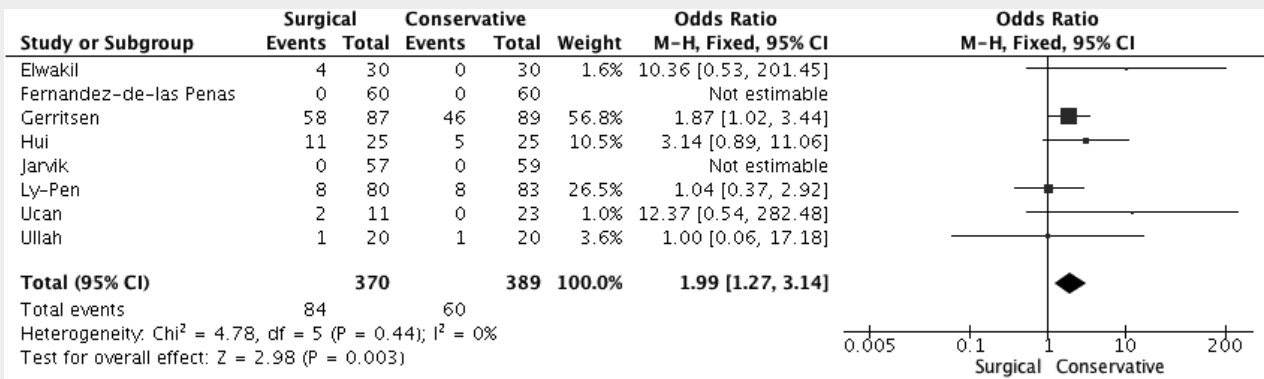


Fig. 6. OR (95%CI) of effect of surgical and conservative treatment on complications reported by pooling data from eight studies ($n = 759$).

also Tables C.11–C.13 in Appendix C for details of included studies).

Side effect and complication

Eight of the trials included reported side effects from treatment. However, there was a wide range of side effects and complications reported. Serious complications were only reported in the surgery group and included reflex sympathetic dystrophy^{25,26} and complex regional pain syndrome.²² Mild side effects from both treatments included symptoms like pain, swelling, discomfort and were reported in most CTs.^{20,22,24,26,30,33,34} The results from 370 wrists, which underwent surgery and 389 wrists treated conservatively, showed that conservative treatment was more beneficial than surgery with almost half the complications reported with conservative compared to surgical treatment (OR = 1.99, 95%CI 1.27 to 3.14, $I^2 = 0\%$, $p = 0.44$) (Fig. 6). The results remain similar, if only high quality studies^{17,18,22,24} were included in the meta-analysis (OR 2.07, 95%CI 1.20 to 3.57, $I^2 = 0\%$, $p = 0.47$) (see Fig. C.3 in Appendix C).

Publication bias

There was symmetry in the funnel plots about the standard error. Therefore, no publication bias was identified because the funnel plots for symptom improvement, functional improvement or improvement of neurophysiological parameters, were symmetric. No publication bias was noted on funnel plots and Egger regression ($p > 0.05$).

Sensitivity analyses

Sensitivity analyses showed that the pooled estimates of outcome measures did not vary substantially with the exclusion of low quality study.

Qualitative analysis and meta-analysis agreement

A comparison of a qualitative analysis and a quantitative analysis (meta-analysis) was only possible where sufficient data were available for a meta-analysis. It is worth noting that there was a considerable agreement between the qualitative and the quantitative analysis, despite the inclusion of different studies in each type of analysis. In particular, the outcomes with conflicting results in the qualitative analysis showed non-significant results in the meta-analysis at the same intervals of reassessment. Furthermore, the outcomes demonstrating statistically significant results in the meta-analysis had strong evidence in favor of a treatment.

Discussion

Even with the inclusion of more recent studies, the results of this systematic review are consistent with the previous systematic reviews with regards to the direction of results. Surgical treatment outweighed conservative treatment in all outcomes. Conservative treatment however caused fewer complications than surgery. Both treatments were effective in improving symptoms and function at six months.

There was some concordance in the results of this systematic review compared to the latest one,¹⁰ with statistically significant results at six months for symptom improvement. There was a disagreement regarding the results at 12 months, with the current meta-analysis showing no significant differences in symptoms and function, in contrast to the previous systematic review, which clearly supported surgery. These differences are attributed to the inclusion of both additional and different studies in the meta-analysis. One trial²⁶ was excluded for reasons previously mentioned, and the most recent study²⁸ showed no difference between the two interventions at 12 months.

The exclusion of low quality trials, for meta-analysis purposes, was only possible for 6 months symptom improvement, 6 and 12 months functional improvement and complication and side effects. The results were only differentiated in functional improvement but this increased the heterogeneity by almost 20%.

Since the heterogeneity of the studies included in the meta-analysis was high, a qualitative analysis was carried out in addition to the meta-analysis. The qualitative analysis allowed for a wider inclusion of studies, upon which to draw conclusions. In addition, it provided a classification of studies according to their quality, with the highest quality studies having a greater effect on the overall outcome. The qualitative analysis took into account the result of each study for each outcome, the methodological quality of each study and the number of studies in favor of an intervention for each outcome.

In the results for symptom improvement, it was evident that surgery was superior to conservative treatment at six months. Regarding functional status at six months, the surgery group had greater functional improvement, which spread to the 12-month re-evaluation (only in the qualitative analysis). However, the results for symptoms and function at three months did not favor one of the interventions as the qualitative analysis showed conflicting evidence and the meta-analysis showed a trend towards surgery, which was not statistically significant.

The reason for this discrepancy between the short- and long-term efficacy for symptoms and function is the use of steroid injections as conservative treatment intervention in the above studies. Steroid injections can reduce wrist joint effusion and

vascular congestion³⁵ around a median nerve which often appears swollen when examined with ultrasound.³⁶ Injections can provide short-term analgesia but the mechanical compression persists,²⁴ resulting in a gradual recurrence of symptoms.

It was previously reported that 50% of the cases treated with steroid injections are worse regarding their clinical presentation and neurophysiological studies over a period of six months.³⁷ This is reflected in the studies using steroid injections used in this review.^{20,22,25,33,34} Ly-Pen *et al.*³³ revealed that as the time passes from the injection until the re-evaluation, the failures of the intervention increase. They attributed the need for review of the original study to this event, and monitored the patients for another year after their initial intervention, where the results were clearly in favor of surgery. On the contrary, surgery provides a more permanent solution, as the resection of the flexor retinaculum decompresses the median nerve. This fact, combined with the complications of surgery, the postoperative discomfort and the patient's reluctance to move after surgery to avoid irritation of the wound, results in a conservative treatment with injections appearing more effective than surgery in the short term.

An additional reason for this discrepancy was the inclusion of the most recent study,²⁸ which affected the overall result at 12 months as it showed no significant differences at 6 and 12 months. The unique feature of this study, which had the highest methodological score (8/11), was the nature of the intervention, which was not concentrated on the wrist, unlike the other conservative interventions. This manual therapy intervention included desensitization maneuvers, across the continuum of the median nerve from the cervical spine to the wrist. Specifically, treatment targeted all possible locations of entrapment of the median nerve along its path, prior to the application of gliding movements of the nerve to improve its glide in relation to the adjacent tissues. This study only included female participants but it is unlikely that the results will be different if participants of both genders were included.

The improvement of neurophysiological parameters was also superior with surgical treatment. The meta-analysis data for DML were extracted from studies with different time intervals, but this was the only way to group the studies together for the meta-analysis.

Complications and side effects were the only occasion where conservative treatment outweighed surgery with almost twice as many complications in the surgery group compared to the group of conservative treatment. Severe complications occurred only with surgery. Most reported side effects were related to pain or tenderness at the incision site, which are common signs and symptoms after open surgery. In addition, there was great heterogeneity in the reported side effects. Only a few studies reported serious side effects, while others reported all adverse reactions regardless of severity. Because there was great variation in the severity of complications reported in each study, it is not possible to verify the real advantage of conservative versus surgical treatment in this outcome.

Additional heterogeneity existed, regarding the chronicity and severity of symptoms, the period of re-evaluation, the outcome measures of each study, and how these were measured. Analysis into subgroups according to the severity of symptoms or the time of reassessment was not possible due to the limited number of studies classifying the patients accordingly. Perhaps, this should be addressed in future trials comparing the two interventions.

The severity of the symptoms could not be accurately determined as there was great variation in the assessment methods. Moreover, some studies^{29–31} did not confirm the diagnosis through electrodiagnostic studies, and as a result, some of the patients included may not have been suffering from CTS alone. The need for neurophysiological studies however is not universally accepted. Some studies indicate that the nerve conduction studies are not necessary for the diagnosis of CTS, since it can lead to false negative or false positive results.^{38–40} Other studies indicate that there is no correlation between clinical symptoms and results of neurophysiological studies in CTS. Researchers propose the use of neurophysiological studies as an additional independent tool for diagnosis and assessment of the severity of CTS.⁴¹

Regarding the severity of the condition, most studies excluded patients with severe atrophy of the thenar muscles, or previous surgery for CTS excluding in this way severe cases of CTS. Six RCTs and CTs reported that they included people with mild to moderate CTS.^{20,23,24,26,33,34} One study included patients with mild, moderate or severe CTS²⁸ and the remaining eight studies

did not make such a reference. Instead, some presented baseline measurements for the severity of symptoms and functional status. Comparing these baseline values from the BQ showed that the severity of symptoms and functional status were comparable between studies, where the severity of CTS is mentioned (see [Tables C.14](#) and [C.15](#) in [Appendix C](#)). Therefore, we can deduce that this systematic review refers mainly to people with mild to moderate CTS.

An additional issue of concern was the fact that the search strategy for this review was limited to electronic databases and the gray literature (unpublished studies) was not searched. This could have affected the results of the publication analysis.

From the studies included, many were limited by lack of randomization, lack of standardized outcome measures and retrospective design, which lacked information on patient baseline measurements, so a comparison of the severity of initial symptoms was not possible, nor was an estimate of the improvement from baseline until reassessment. The incorporation of prospective and retrospective studies however allowed for an evaluation of the outcomes in the longer term.

In the absence of randomization, these observational studies are considered lower quality than RCTs and CTs for the collection of data on the efficacy of an intervention because they can be affected by various types of bias such as selection, detection, performance, attrition, reporting and publication.¹⁵ However, their inclusion constituted a strength of this review. In these studies, treatment was pre-determined according to the severity of the condition. Patients with severe CTS underwent surgery. Since the surgical intervention was more effective than conservative, and in more severely impaired patients, one can assume that the effect size of surgery might be higher than the one of the conservative. On the other hand, a long-term observational study⁴² presented evidence that in some cases, CTS may improve spontaneously, causing these patients to undergo unnecessary surgery. In addition, severely impaired patients might find it easier to score positively on subjective outcome measures like VAS and GSS. These remarks make the formulation of a clear conclusion difficult and future studies should address them.

An evaluation of 331 hands identified 5 factors of poor prognosis and the need for surgery: age above 50 years, symptom for over 10 months,

consecutive symptoms of paraesthesia, flexor tenosynovitis and a positive Phalen's test for less than 30 s.⁴³ It was reported that when these factors did not exist, 2/3 of patients healed with conservative treatment. When 4 or 5 of these factors are present, they recommend surgical treatment. Conversely, other researchers studied 45 hands conservatively with steroid injections and concluded that there is no correlation between signs and symptoms of CTS and the final result.⁴⁴ They argued that chronicity is the most significant factor for the final result.⁴⁴ Therefore, conservative treatment is a feasible option for mild and short-term symptoms, but surgery can provide a more permanent solution to persisting symptoms.

Conclusion

The results of this review demonstrate that surgery leads to a greater improvement of symptoms and neurophysiological parameters at six months, compared to conservative treatment. The decision however, about the choice of treatment, needs careful consideration, taking into account the complications reported with surgical treatment and the fact that in some cases, CTS may be resolved spontaneously. However, the conclusions derived from this review are based on a number of underpowered studies. Therefore, high quality prospective studies are needed in order to identify the characteristics of individuals where CTS has promising path to avoid unnecessary surgery. In addition, further research should focus on exploring the field of manual therapy and compare it to the surgical intervention for CTS. Research should also address the long-term effectiveness of the two interventions beyond 12 months.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Author Contributions

DK was responsible for the data collection, data analysis, data interpretation and writing the manuscript, IM was responsible for revising the manuscript, statistical analysis and project management. Both authors participated in editing and completion of the manuscript.

Appendix A.

Summary of search strategy.

#	Keywords	PubMed (Title/ Abstract)	EBSCO (Abstract)
#1	((surgical*) OR (surgical intervention) OR (open carpal tunnel release) OR (OCTR) OR (endoscopic carpal tunnel release) OR (ECTR))	822.822	1.713.262
#2	((conservative) OR (conservative intervention) OR (corticosteroid injections) OR (steroid injections) OR (wrist splints) OR (physiotherapy) OR (electrotherapy) OR (exercise) OR (manual therapy))	322.464	1.579.763
#3	((Carpal tunnel syndrome) OR (CTS) OR (median nerve entrapment) OR (nerve compression))	13.486	61.818
#4	((RCT) OR (random*) OR (randomized controlled trial) OR (controlled trial) OR (cohort study) OR (clinical trial) OR (controlled clinical trial) OR (retrospective) OR (prospective))	1.595.404	6.814.297
#5	#1 AND #2 AND #3 AND #4	72	387

Appendix B.

List of excluded papers

Study	Year	Title	Reason for exclusion
Martin <i>et al.</i>	2005	RCT of surgery versus conservative therapy for CTS	Study protocol
Schrijver <i>et al.</i>	2005	Correlating nerve conduction studies and clinical outcome measures on CTS: Lessons from a randomized controlled trial	Study comparing nerve conduction and clinical improvement using the data from the study of Ref. 26
Korthals-de Bos <i>et al.</i>	2006	Surgery is more cost-effective than splinting for CTS in the Netherlands: Results of an economic evaluation alongside a randomized controlled trial	Cost-effectiveness study using the data from Ref. 26
Pomerance <i>et al.</i>	2009	The cost-effectiveness of non-surgical versus surgical treatment for CTS	Cost-effectiveness study
Vogelin <i>et al.</i>	2010	Sonographic follow-up of patients with CTS undergoing surgical or non-surgical treatment: Prospective cohort study	Different outcome measures. Study measuring the size of the carpal tunnel after the intervention.
Onuma <i>et al.</i>	2013	Bilateral CTS due to gouty tophi: Conservative and surgical treatment in different hands of the same patient	Case-control study

Appendix C.

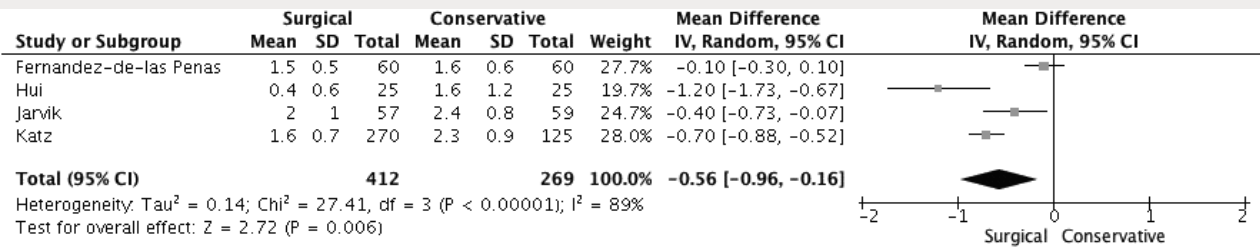


Fig. C.1. Detailed meta-analysis results for symptom improvement if only high quality studies^{17,18,22,26} were included.

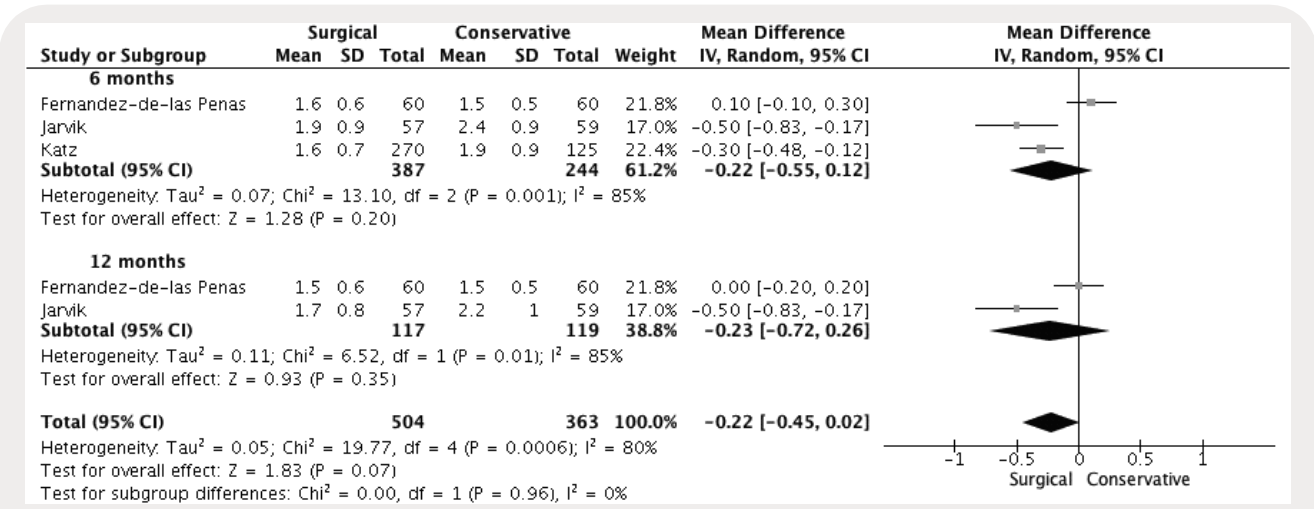


Fig. C.2. Detailed meta-analysis results for functional improvement at 6 and 12 months if only high quality studies^{17,18,26} were included.

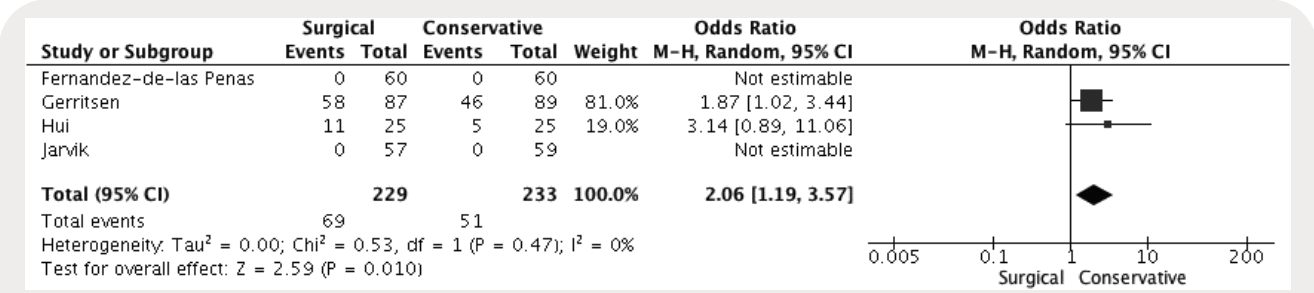


Fig. C.3. OR (95%CI) of effect of surgical and conservative treatment on complications reported if only high quality studies^{17,18,26} were included.

Table C.1. Qualitative analysis (symptom improvement — 3 months).

	Favors surgery	No difference	Favors conservative
High quality	Ref. 26	Ref. 28	
Low quality	Ref. 25	Ref. 26	Refs. 20 and 22

Table C.3. Qualitative analysis (symptom improvement — 12 months).

	Favors surgery	No difference	Favors conservative
High quality	Refs. 26 and 27	Ref. 28	
Low quality		Ref. 20	

Table C.2. Qualitative analysis (symptom improvement — 6 months).

	Favors surgery	No difference	Favors conservative
High quality	Refs. 24, 26 and 27	Ref. 28	
Low quality	Refs. 22, 26 and 30	Ref. 20	

Table C.4. Qualitative analysis (symptom improvement — 18 months).

	Favors surgery	No difference	Favors conservative
High quality	Refs. 26 and 31*		
Low quality			

Note: *Observational study.

Table C.5. Qualitative analysis (symptom improvement — >18 months).

	Favors surgery	No difference	Favors conservative
High quality	Ref. 31*		
Low quality	Refs. 29 and 33	Ref. 21	

Note: *Observational studies.

Table C.10. Qualitative analysis (functional improvement — >18 months).

	Favors surgery	No difference	Favors conservative
High quality	Ref. 31		
Low quality	Refs. 29* and 33		

Note: *Observational studies.

Table C.6. Qualitative analysis (functional improvement — 3 months).

	Favors surgery	No difference	Favors conservative
High quality		Ref. 26	Ref. 28
Low quality		Ref. 23	Refs. 20 and 22

Table C.11. Qualitative analysis (improvement of neurophysiological parameters — 3 months).

	Favors surgery	No difference	Favors conservative
High quality			
Low quality		Ref. 23 (apart from SNCV and DSL) and Ref. 22	

Table C.7. Qualitative analysis (functional improvement — 6 months).

	Favors surgery	No difference	Favors conservative
High quality	Refs. 24, 26, 27 and 31*	Ref. 28	
Low quality	Ref. 23	Refs. 20 and 22	

Note: *Observational study.

Table C.12. Qualitative analysis (improvement of neurophysiological parameters — 6 months).

	Favors surgery	No difference	Favors conservative
High quality		Ref. 24 (apart from SNCV)	
Low quality		Ref. 23 (apart from SNCV and DSL), Refs. 22 and 30	

Table C.8. Qualitative analysis (functional improvement — 12 months).

	Favors surgery	No difference	Favors conservative
High quality	Refs. 26 and 27	Ref. 28	
Low quality	Ref. 20		

Table C.9. Qualitative analysis (functional improvement — 18 months).

	Favors surgery	No difference	Favors conservative
High quality	Ref. 31*	Ref. 26	
Low quality			

Note: *Observational study.

Table C.13. Qualitative analysis (improvement of neurophysiological parameters — 12 months).

	Favors surgery	No difference	Favors conservative
High quality	Ref. 26 (apart from DSL)	Ref. 26 (apart from DML)	
Low quality	Refs. 21* and 34		

Note: *Observational study.

Table C.14. Symptom severity baseline measurements.

Study	Measurement tool	Intervention	Baseline measurement
Ref. 31	Symptom severity scale	Surg:	3.2 ± 0.8
		Cons:	2.6 ± 0.8
Ref. 23	BQ	Surg:	3.4 ± 0.7
		Cons:	3.3 ± 0.7
Ref. 26	Symptom severity scale	Surg:	2.5 (1.9–3.1)
		Cons:	2.4 (1.8–2.9)
Ref. 24	GSS/10	Surg:	2.86 ± 1.10
		Cons:	2.52 ± 1.05
Ref. 22	BQ	Surg:	3.09 ± 0.5
		Cons (Splinting):	2.66 ± 0.35
		Cons (Splint + injection):	2.79 ± 0.63
Ref. 27	CTSAQ	Surg:	2.95 ± 0.77
		Cons:	3.01 ± 0.64
Ref. 25	GSS/10	Surg:	3.545 ± 0.74
		Cons:	3.48 ± 0.81
Ref. 28	BQ	Surg:	2.7 ± 0.6
		Cons:	2.5 ± 0.7

Table C.15. Functional status baseline measurements.

Study	Measurement tool	Intervention	Baseline measurement
Ref. 31	Functional status scale	Surg:	2.7 ± 0.9
		Cons:	2.1 ± 0.9
Ref. 23	BQ	Surg:	3.3 ± 1.0
		Cons:	3.0 ± 0.8
Ref. 26	Functional status scale	Surg:	2.3 (1.5–3.0)
		Cons:	2.0 (1.5–2.9)
Ref. 20	VAS scale/20	Surg:	1.95 ± 1.40
		Cons:	1.895 ± 1.318
Ref. 22	BQ	Surg:	2.7 ± 0.62
		Cons (Splinting):	2.47 ± 0.65
		Cons (Splint + injection):	2.19 ± 0.51
Ref. 27	CTSAQ	Surg:	2.42 ± 0.82
		Cons:	2.53 ± 0.82
Ref. 28	BQ	Surg:	2.4 ± 0.6
		Cons:	2.3 ± 0.5

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