Surgical versus non-surgical treatment for carpal tunnel syndrome (Review)

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[Intervention review]

Surgical versus non-surgical treatment for carpal tunnel syndrome

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ABSTRACT

Background

Carpal tunnel syndrome results from entrapment of the median nerve in the wrist. Common symptoms are tingling, numbness, and pain in the hand that may radiate to the forearm or shoulder. Most symptomatic cases are treated non-surgically.

Objectives

The objective is to compare the efficacy of surgical treatment of carpal tunnel syndrome with non-surgical treatment.

Search strategy

We searched the Cochrane Neuromuscular Disease Group Trials Register (January 2008), MEDLINE (January 1966 to January 2008), EMBASE (January 1980 to January 2008) and LILACS (January 1982 to January 2008). We checked bibliographies in papers and contacted authors for information about other published or unpublished studies.

Selection criteria

We included all randomised and quasi-randomised controlled trials comparing any surgical and any non-surgical therapies.

Data collection and analysis

Two authors independently assessed the eligibility of the trials.

Main results

In this update we found four randomised controlled trials involving 317 participants in total. Three of them including 295 participants, 148 allocated to surgery and 147 to non-surgical treatment reported information on our primary outcome (improvement at three months of follow-up). The pooled estimate favoured surgery (RR 1.23, 95% CI 1.04 to 1.46). Two trials including 245 participants described outcome at six month follow-up, also favouring surgery (RR 1.19, 95% CI 1.02 to 1.39).

Two trials reported clinical improvement at one year follow-up. They included 198 patients favouring surgery (RR 1.27, 95% CI 1.05 to 1.53). The only trial describing changes in neurophysiological parameters in both groups also favoured surgery (RR 1.44, 95% CI 1.05 to 1.97). Two trials described need for surgery during follow-up, including 198 patients. The pooled estimate for this outcome

indicates that a significant proportion of people treated medically will require surgery while the risk of re-operation in surgically treated people is low (RR 0.04 favouring surgery, 95% CI 0.01 to 0.17). Complications of surgery and medical treatment were described by two trials with 226 participants. Although the incidence of complications was high in both groups, they were significantly more common in the surgical arm (RR 1.38, 95% CI 1.08 to 1.76).

Authors' conclusions

Surgical treatment of carpal tunnel syndrome relieves symptoms significantly better than splinting. Further research is needed to discover whether this conclusion applies to people with mild symptoms and whether surgical treatment is better than steroid injection.

PLAIN LANGUAGE SUMMARY

Surgical versus non-surgical treatment for carpal tunnel syndrome

Carpal tunnel syndrome is caused by compression of the median nerve which goes through the carpal tunnel in the wrist. It causes tingling, numbness and pain, mostly in the hand. Treatment is controversial. This review aimed to compare surgical decompression with non-surgical treatments such as splinting or corticosteroid injections. Four trials were found and included, while three are awaiting assessment. The results suggest that surgical treatment is probably better than splinting but it is unclear whether it is better than steroid injection. Further research is needed for those with mild symptoms.

BACKGROUND

Carpal tunnel syndrome (CTS) is the clinical condition resulting from entrapment of the median nerve where it passes under the transverse carpal ligament in the wrist. This region is a closed space within which pressure may rise. Thickening of tendon sheaths or encroachment by other structures leads to a sustained rise in pressure within the canal. This pressure is further increased by flexion or extension of the wrist (Dawson 1999). Carpal tunnel syndrome has been accepted as the most common entrapment neuropathy (Stewart 1993; Martyn 1997). Cross-sectional studies in the Netherlands suggest a prevalence of 9.2% in the female and 0.6% in the male population (de Krom 1992). It has an important economic impact, affecting active people and may occur as a work-related disorder (Rossignol 1997) leading to compensation claims (Leigh 1998).

The most common symptoms are tingling, numbness and pain within the median nerve distribution (particularly the thumb, index and middle fingers) worsening at night. Pain may radiate proximally to the forearm or shoulder. On examination, there may be weakness and atrophy of the thenar muscles associated with sensory loss in the affected fingers.

In spite of the public health importance of CTS, there are no universally accepted diagnostic clinical and laboratory criteria. However, it is agreed that certain electrophysiological abnormalities support the diagnosis. The most frequently used parameters are distal motor and sensory latencies as well as the sensory conduction velocity across the carpal tunnel (Stevens 1997). Other techniques such as a comparison between the distal sensory or motor latencies stimulating the ulnar and median nerve (Felsenthal 1977) or the radial and median nerves (Carroll 1987) have been used. The 'inching technique' (Kimura 1979) allows a precise localisation of the site of entrapment, but its clinical relevance is under debate (Geiringer 1998). There is no universally accepted therapy for CTS (Rosenbaum 1993) although clinical guidelines have been suggested (AAN 1993). For symptomatic patients a range of treatment is offered varying widely around the world, within individual countries, and even hospitals. Most patients are treated non surgically (Miller 1994).

This is an update of a systematic review aiming at discovering whether the evidence supports the assumed therapeutic benefit of surgery over non-surgical treatment. Due to the lack of agreement regarding the criteria for diagnosis of CTS, all studies of symptomatic patients including a control group were to be considered regardless of the diagnostic criteria applied. Subgroup analysis of those trials using the American Academy of Neurology practice parameter for the diagnosis of CTS (AAN 1993) were to be performed if data had been available. Non-surgical therapies such as wrist splints, modification of activities, non-steroidal anti-inflammatory drugs, diuretics and steroid injection into the carpal tunnel (AAN 1993), were to be considered as valid comparisons with the surgical group. Because there is no universally accepted surgical technique for the treatment of this condition, all procedures such as open or endoscopic section of transverse carpal ligament, with or without neurolysis were to be included. The comparison of the therapeutic effect of different surgical techniques is the subject of a parallel systematic review (Scholten 2007).

OBJECTIVES

The objective of this review is to compare the efficacy of surgical treatment of CTS with non-surgical treatment in improving clinical outcome.

METHODS

Criteria for considering studies for this review

Types of studies

We intended to include all published and unpublished studies in any language, attempting to compare surgical treatment with either non-surgical or no treatment in a randomised way, irrespective of the quality of randomisation and blindness of the design.

Types of participants

All participants diagnosed with CTS were included irrespective of the diagnostic criteria used, aetiology of the syndrome, associated pathology, gender and age.

Types of interventions

All surgical techniques were included and all non-surgical treatments were considered.

Types of outcome measures

Primary outcomes

The primary outcome measure was relevant clinical improvement after three months of follow-up. The improvement was considered relevant if it implied significant relief of pain and paraesthesiae, by at least 50% of the baseline level (Verdugo 1994), or improvement of hypoaesthesia or muscle weakness resulting in improvement in quality of life and functional status.

Secondary outcomes

1. Improvement of neurophysiological parameters.
2. Clinical improvement reported by authors without including its relevance to the functional status of the participant, for example better performance with the two point discrimination test.
3. Clinical improvement at less than three months of follow-up.
4. Clinical improvement at one year of follow-up.
5. Complications of surgery including formation of a painful neuroma of the palmar cutaneous branch of the median nerve, tender or hypertrophic scar, section of the motor branch, subluxation ('bow stringing') of flexor tendons, wound infection and reflex sympathetic dystrophy.
6. Need for surgery during follow-up in participants treated medically or secondary surgery in those treated surgically.
7. Complications of medical treatments, particularly steroid injections. These include among others damage to the median nerve, chemical synovitis, infection and digital flexor tendon rupture.
8. Return to work at three months or less of follow-up.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Neuromuscular Disease Group Trials Register for randomised trials using 'median nerve entrapment', 'carpal tunnel syndrome' and 'entrapment neuropathy' as the search terms. We originally searched MEDLINE and EMBASE and the LILACS database. LILACS is a specialised database, supported by the Pan-American Health Organisation, aiming to collect all biomedical literature published in Latin America.
We updated the search of the Cochrane Neuromuscular Disease Group Trials Register (January 2008), MEDLINE (January 1966 to January 2008), EMBASE (January 1980 to January 2008) and LILACS (January 1982 to January 2008), which revealed two further relevant trials.
For full search strategies for each of the databases listed above, see Appendix 1,Appendix 2 and Appendix 3.

Searching other resources

We checked the bibliographies in relevant papers and contacted the authors to obtain information about other published or unpublished studies.

Data collection and analysis

A search was conducted to identify new trials not included previously, to update this review. The abstracts were read by two authors independently (RS and RV). Any disagreement about inclusion of a study would have been discussed with a third author (JGC) and a consensus reached. Data were extracted independently by three authors (RV, RS and JGC) using a structured sheet. Any disagreement would have been discussed by the complete group of authors to reach a consensus. Statistical analysis was performed using the Review Manager (RevMan) software developed by the Cochrane Collaboration. Both proportional and absolute risk reductions were calculated for each outcome. Heterogeneity between trial results was tested with a standard Chi squared test. The main analysis was based on consideration of all included trials. Trials with good allocation concealment would also have been analysed separately (Schulz 1995). We also planned a priori sensitivity analyses based on:

1. gender and
2. diagnostic criteria (trials using the diagnostic criteria proposed by the AAN (AAN 1993) and those which did not).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting assessment.
We found four randomised controlled trials (Garland 1964 ; Gerritsen 2002; Ly Pen 2005; Hui 2005). One of them (Garland 1964) included 22 women diagnosed with CTS based on clinical evaluation and distal motor latency of the median nerve greater than 4.5 milliseconds, although the distance between distal stimulating and recording sites was not given. Participants were allocated to one of two groups by a secretary, using 'a previously prepared random list'. One group had open section of the anterior carpal ligament; the other had splinting 'of the hand, wrist and arm for one month'. Eleven participants were allocated to each arm. One participant allocated to the surgical arm refused surgery, but was included by us in the originally allocated group. The other 11 participants underwent splinting. Both groups of participants 'were

reviewed clinically and electromyographically at regular intervals for up to one year,' and outcomes were given for the end of this period of follow-up. Another study (Gerritsen 2002) included 143 women and 33 men out of 326 participants examined for eligibility. The diagnosis of CTS was based on clinical evaluation and electrophysiological findings (decreased sensory conduction velocity in the median nerve or an increased median-ulnar distal sensory latency difference). Participants were allocated to overnight splinting of the wrist for at least six weeks, or open surgical release of the carpal tunnel ligament, using a block randomisation method stratified by centre. The sequence was generated using random number tables. Eighty-seven participants were allocated to surgery and 89 to splinting. Fourteen participants allocated to surgery and 13 participants allocated to splinting did not receive the treatment as assigned. Both groups of participants were evaluated by a physiotherapist at baseline and at three, six and twelve months after randomisation. Clinical improvement was evaluated using a six-point ordinal scale. Two further primary outcomes were considered: number of nights that the participant awoke due to the symptoms during the past week and the severity of the main complaint. A third study (Ly Pen 2005) included 93 women and 8 men. This study considered wrists, rather than patients, as the unit of randomisation. Patients with bilateral CTS were included, undergoing separate randomisation for each wrist. They thus report that 163 out of 217 "wrists" eligible for randomisation, were included. In the published paper they report a subgroup analysis of outcome in 69 patients with either unilateral CTS or in the most symptomatic wrist in patients with bilateral CTS. These are the patients included in our statistical analysis. Patients were 18 years old or older. Inclusion criteria were symptoms of CTS of at least three months, unresponsive to a course of at least two weeks of nonsteroidal anti-inflammatory drugs and splinting. They were enrolled only if clinical and electrophysiological features of CTS were present (distal motor latency in the median nerve above 4.2 msec or a decrease in the sensory conduction velocity at the carpal tunnel below 44 m/sec.). Patients were allocated to open surgery or steroid injection beneath the transverse carpal ligament from the ulnar side of the wrist. For the subgroup of patients included in our meta-analysis, the authors reported a 70% improvement in nocturnal paraesthesias at three, six and twelve months. They reported that "results for 20% and 50% improvement in the three domains were similar". The fourth study (Hui 2005) included 48 women and 2 men out of 63 patients examined for eligibility. Patients with newly diagnosed CTS of more than three months but less than one year of duration were enrolled if clinical and electrophysiological features of CTS were present. The electrophysiological criteria were: median-ulnar palmar sensory latency difference greater than 0.5 msec. or distal motor latency (DML) greater than 4.0 msec. Severe CTS with thenar atrophy or unobtainable DML were excluded. Patients were randomly allocated by a computer-generated code to surgical decompression of the carpal tunnel (by one experienced neurosurgeon), under local anaesthesia or steroid injection. The primary outcome considered was improvement in symptoms as measured by the global symptom score (GSS) 20 weeks after intervention. GSS rates symptoms on a scale of 0 (no symptoms) to 10 (severe) in five categories: pain, numbness, paraesthesia, weakness/clumsiness, and nocturnal awakening (Hui 2005). They considered as secondary outcomes, electrophysiological measures (DML and sensory nerve conduction velocity) and grip strength measurements using a dynamometer.

Risk of bias in included studies

The four included studies stated that participants were allocated randomly, although in one of them (Garland 1964) it is not clear how the randomisation sequence was generated, or if it was properly concealed. The fact that the 22 participants turned out to be distributed in even sets of eleven, raises doubts about the quality of the randomisation and allocation concealment but we do not have evidence to support this suspicion. No losses to follow-up were reported. The other three studies (Gerritsen 2002; Hui 2005; Ly Pen 2005) had adequate allocation concealment since the allocated treatment was included in a coded and sealed opaque envelope. In the surgical arm of one of them (Gerritsen 2002) there were nine participants (10.3 %) not included in the analysis at three months of follow-up and 14 (16 %) at one year. In the non-surgical arm three participants (3.3 %) were not included in the analysis at three months and six (6.6%) at twelve months. In the third study (Ly Pen 2005) there were no losses to follow-up at three months, which is the time of our primary outcome, while they reported in the surgical group one "wrist" loss at six months and four additional "wrists" at twelve months of follow-up. In the injection wrist group they reported two "wrists" lost to follow-up at twelve months. The authors of the fourth study (Hui 2005) reported no losses to follow up.

Two of the four studies were not blinded (Garland 1964; Ly Pen 2005). Two of them (Gerritsen 2002; Hui 2005) attempted to hide the scar from the evaluators with a plaster.

See Table 1.

Table 1. Methodological quality of included studies

Study	Alloc. concealment	Diagnostic criteria	Baseline differences	Patient blinding	Observer blinding

Table 1. Methodological quality of included studies

(*Continued*)

Garland 1964	unclear	adequate	not reported	not attempted	not attempted
Gerritsen 2002	adequate	adequate	adequate	not attempted	inadequate
Hui 2005	adequate	adequate	adequate	not attempted	inadequate
Ly-Pen 2005	adequate	adequate	adequate	not attempted	not attempted

Effects of interventions

The analyses included all events regardless of the compliance of the participants with the treatment to which they were allocated.

Primary outcome

Three trials (Gerritsen 2002; Ly Pen 2005; Hui 2005) considered relevant clinical improvement after three months. In one of them (Gerritsen 2002) treatment success was defined as completely recovered or much improved using the ordinal scale mentioned above. Out of 87 participants allocated to surgery, 62 (71%) were in these categories at three months. Out of 89 participants allocated to splinting, 46 (51.6%) qualified for treatment success. The confidence interval favoured the surgical group (relative risk (RR) 1.38, 95% confidence interval (CI) 1.08 to 1.75). In the second trial (Ly Pen 2005), out of 33 patients allocated to injection, 29 (87.9%) had 70% improvement in nocturnal paraesthesiae while out of 36 patients allocated to surgery 21 (58.3%) obtained the same result, at three months (RR 0.66, 95% CI 0.49 to 0.90). A third trial (Hui 2005) reported clinical improvement publishing averages at baseline, 6 and 20 weeks after intervention. At 20 weeks they published an improvement in the GSS from 25.2 to 16.6 in the injection group, and from 28.6 to 4.3 in the surgical group. The corresponding author sent us the raw data showing that in the injection group 11 out 25 patients improved by at least 50% in the GSS while in the surgical group 24 out of 25 improved by 50% or more at 20 weeks (RR 2.18, 95% CI 1.39 to 3.42). The meta-analysis gave a pooled estimate of RR 1.23, CI 1.04 to 1.46 favouring surgery (see Analysis 01.01).

Two trials (Gerritsen 2002, Ly Pen 2005) also considered clinical improvement at six months. In the first (Gerritsen 2002) seventy-two participants (82.7%) from the surgical group showed significant clinical improvement while 57 participants (64%) in the non-surgical group did so. The CI favoured the surgical group (RR 1.29, 95% CI 1.08 to 1.55). In the second (Ly Pen 2005) 24 patients (72.7%) in the injection group and 25 (69.4%) in the surgical group achieved a 70% response in nocturnal paraesthesiae (RR 0.95, 95% CI 0.71 to 1.29). The pooled estimate from all three trials was RR 1.19, 95% CI 1.02 to 1.39, again favouring surgery (see Analysis 01.02).

Secondary outcome

(1) Clinical improvement at one year of follow-up

In one trial (Garland 1964) all the patients operated upon in the trial were completely relieved of symptoms for at least one year,' while only two participants allocated to the non-surgical group 'were relieved temporarily'. Although for these two participants an exact time period was not given, we considered them as being relieved of symptoms for at least one year. The result favoured the surgical group (RR 5.00, 95% CI 1.41 to 17.76). The other trial (Gerritsen 2002) reported significant improvement at one year in 67 out of 87 patients (77%) in the surgical group, and 60 out of 89 (67.4%) in the non-surgical group, favouring surgery (RR 1.14, 95% CI 0.95 to 1.37). The pooled estimate favoured surgery (RR 1.27, 95% CI 1.05 to 1.53) (see Analysis 02.01). A third trial (Ly Pen 2005) reported a non significant difference favouring surgery, in nocturnal paraesthesiae, at 12-month follow-up (63.6% of wrists in the injection group and 69.4% in the surgery group achieved a 70% response).

(2) Clinical improvement reported by authors without including its relevance to the functional status of the participant

One trial (Hui 2005) reported improvement in grip strength at 20-week as measured by a trained occupational therapist using a JAMAR hydraulic hand dynamometer. The results favoured the non-surgical group without reaching statistical significance (RR 0.71, 95% CI 0.43 to 1.15) (see Analysis 02.02).

(3) Improvement of neurophysiological parameters

One trial (Garland 1964) described complete reversal of the neurophysiological abnormalities in all operated participants but this outcome was not described in the non-operated participants, preventing the comparison between the two groups. A second trial (Gerritsen 2002) reported improvement in distal sensory latency in the median nerve, median-ulnar distal sensory latency difference, and distal motor latency in the distal nerve in both treatments groups. However, only average figures were given, preventing us from calculating the differences in risks between both groups. A third trial (Hui 2005) reported improvement in DML and sensory

nerve conduction after both interventions greater in the surgical group. In the surgical group 23 out of 25 patients showed improvement in amplitude of sensory potential while 16 out of 25 in the injection group did so (RR 1.44, 95% CI 1.05 to 1.97) (see Analysis 02.06).

(4) Need for surgery during follow-up in participants treated medically or secondary surgery in those treated surgically

In one trial (Garland 1964) among the 11 participants treated medically, eight underwent surgery during follow-up. Apparently no operated participant required re-operation, although no information was given regarding secondary surgeries. The result favoured the surgical group (RR 0.06, 95% CI 0.00 to 0.91). In other series (Gerritsen 2002) one out of 87 participants in the surgical group underwent re-operation and 35 out of 89 participants in the splinting group underwent surgery (RR 0.03, 95% CI 0.00 to 0.21). The pooled estimate indicated that a significant proportion of medically treated people required surgery while the risk of re-operation in the surgically treated people is low: RR 0.04, 95% CI 0.01 to 0.17 (see Analysis 02.03). The other two trials (Ly Pen 2005; Hui 2005) did not report need for surgery in the injection group or need for a second surgery in the surgical group.

(5) Clinical improvement at less than three months of follow-up

One trial (Gerritsen 2002) reported relevant clinical improvement at one month of follow-up. Twenty-three out of 87 participants (26.4%) assigned to undergo surgery, and 37 out of 89 participants in the non-surgical group (41.5%) showed significant improvement. This outcome favoured non-surgical treatment (RR 0.64, 95% CI 0.41 to 0.98) (see Analysis 02.04).

(6) Complications of surgery and medical treatment

Secondary outcomes (5) and (6), as stated in the methods, were merged for the purpose of this analysis. One of the trials (Gerritsen 2002) reported adverse effects during the follow-up period. Adverse effects include painful or hypertrophic scar; wound haematoma and infection; stiffness, swelling or discomfort of the wrist and reflex sympathetic dystrophy. Fifty-eight out of 87 participants (56.6%) allocated to surgery and 46 out of 89 participants (51.7%) in the non-surgical group had at least one adverse effect. The authors did not describe major complications such as damage to a nerve and a significant proportion of complications in the group assigned to splinting were attributed to surgery needed during the follow-up. Another series (Hui 2005) reported no major surgical complications; there were two wound haematomas and nine cases of mild to moderate wound pain in the surgical group while in the injection group there were one case of cellulitis and four cases of pain at the injection site. The pooled results favoured non-surgical treatment (RR 1.38, 95% CI 1.08 to 1.76) (see Analysis 02.05).

DISCUSSION

In this update, we included four randomised controlled trials comparing surgical and non-surgical therapies in people diagnosed as suffering carpal tunnel syndrome. These trials indicate that there is a better response from people undergoing surgical treatment compared with splinting (Garland 1964; Gerritsen 2002) but it is unclear whether there is a better response from surgical treatment compared with steroid injection (Ly Pen 2005; Hui 2005). The difference is statistically significant. Detection bias could not be ruled out because of the lack of blinding of the outcome assessment in two trials (Garland 1964; Ly Pen 2005) while the other two (Gerritsen 2002; Hui 2005) attempted to hide the scar with a plaster. In one of the trials (Garland 1964) it is not clear if selection bias was avoided due to the lack of information about the randomisation procedure. Apparently there was a high level of heterogeneity among the participants admitted to this trial, judging from the period of time of symptoms, ranging from one month to twenty years. As there is no information on the baseline clinical and electrophysiological status of the two groups, we cannot be sure that the risk of both groups was similar in this trial. The other three trials had adequate allocation concealment (Gerritsen 2002; Hui 2005; Ly Pen 2005). Significant improvement after three months, defined as the primary outcome in this review, was reported by three trials (Gerritsen 2002; Hui 2005; Ly Pen 2005) favouring surgery with a RR of 1.23 (95% CI 1.04 to 1.46). However, significant statistical heterogeneity exists among the included trials (test for heterogeneity $Chi^2 = 22.96$, df = 2 $p < 0.0001$, $I^2 = 91.3\%$), that may be explained by clinical diversity among trials. Two of these trials favoured surgery (Gerritsen 2002; Hui 2005) and one favoured steroid injection (Ly Pen 2005). A possible cause for the heterogeneity is the fact that in the trial that reported a better outcome for non surgical treatment (Ly Pen 2005), only the subgroup with unilateral STC was included in our analysis. Furthermore this trial considered as inclusion criteria non-respondent patients to medical treatment including splinting. In these trials the participants allocated to surgical and non-surgical groups showed no significant differences in relevant features.

The pooled number of participants included in these trials was adequate to detect differences in improvements between both arms. At the time of collecting data for the primary outcome analysis the losses were 6.08% (9 out of 148 participants) in the surgical group and 2.04% (3 out of 147 participants) in the non-surgical group. A sensitivity analysis assuming that all participants lost to follow-up in the surgical group did not improve and all participants lost in the splinting group improved, did not change the significance of the primary outcome analysis, although the lower limit of the 95% confidence interval for the RR was 1.01. Both treatment groups had a good success rate in two trials (Gerritsen 2002; Ly Pen 2005) although it should be noted that a large number of patients allocated to splinting in one trial (Gerritsen 2002) underwent surgery during follow-up and the other trial (Ly Pen 2005)

did not report need for surgery during follow up in the injection group. A third trial (Hui 2005) reported good recovery rate in the surgical group but only 44% of patients improving with steroid injection. Even though a subgroup analysis was not specified for different non-surgical treatments, it should be noted that when surgery is compared with steroid injection, the combined results do not clearly favour one intervention over the other, at least for a short-term outcome such as three months symptomatic response.

Only two trials reported adverse effects during the follow up period (Gerritsen 2002; Hui 2005) and these were common in both groups, although a significant number of adverse events reported in the non-surgical group was caused by surgery during follow-up. This pooled estimate was based on the intention-to-treat analysis which was confounded by the fact that many participants in the non surgical group had received surgery before the one year follow-up visit. Most adverse effects in the non surgical group were reported by one trial (Gerritsen 2002). The frequency of adverse events must be considered by the treating physician when advising on the choice of surgical or non-surgical therapies.

There is insufficient information in the paper reporting better outcome in the splinting group at one month of follow-up (Gerritsen 2002) to draw any meaningful conclusion. The results after one year of follow-up could be analysed including only two trials (Garland 1964; Gerritsen 2002). Both of them suggest that choosing surgery improves the chance of a good outcome. One of them (Garland 1964) shows a statistically significant improvement while the other does not (Gerritsen 2002). The pooled results show an overall better outcome for surgery by about 14%, but it should be noted that the statistical heterogeneity between trials is significant. This heterogeneity may be explained by the clinical and methodological diversity existing among trials. The inclusion of more severely affected patients may explain the better results in the surgical group in one of the trials (Garland 1964). In the earlier trial (Garland 1964) the neurophysiological criterion used was a distal motor latency of the median nerve greater than 4.5 msecs, while in the other trial (Gerritsen 2002) electrophysiological criteria included decreased sensory conduction velocity in the median nerve or an increase median to ulnar sensory latency. These different criteria might have resulted in the inclusion of patients with a lesser degree of severity in the Gerritsen trial (Gerritsen 2002). A further possible reason for the significant heterogeneity between the trials may reside in the high proportion of patients allocated to splinting that ended up undergoing surgery within one year of follow-up in one of the trials (Gerritsen 2002). Furthermore, the trial whose outcomes at one year were not included in the analysis due to the way in which the results were presented (Ly Pen 2005), reported no significant difference between surgical and non-surgical treatments at one year of follow up.

Although the better results in the surgical group are statistically significant, the lower limit of the CI is close to the non significant threshold. The high incidence of adverse events indicates the need to identify subgroups of participants who would be most likely to benefit from surgery. Therefore there is still a need for well designed clinical trials addressing the question of the efficacy of surgery in CTS. These studies should consider age, occupation, duration of symptoms and severity of the entrapment, among others, as criteria to identify subgroups in advance.

AUTHORS' CONCLUSIONS

Implications for practice

Surgical treatment seems to be better than non-surgical treatment for relieving symptoms of carpal tunnel syndrome. The superiority of surgery over splinting seems evident, but this not so clear with steroid injection.

Implications for research

There is a need for further research to assess the effect of operation on functional outcome and in subgroups such as those with mild symptoms. Further studies are also necessary comparing surgery with steroid injection.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Garland 1964

Methods	R = random sequence administered by secretary. Not known if the allocation was properly concealed. No blinding.
Participants	22 women. CTS diagnosed based on clinical evaluation and distal motor latency > 4.5 msec.
Interventions	Surgical intervention by open section of the anterior carpal ligament versus splinting for one month.
Outcomes	Complete relief of symptoms and reversal of neurophysiological parameters.
Notes	UK

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Gerritsen 2002

Methods	R = block randomisation using coded and sealed opaque envelopes. Sequence generated using random number tables.
Participants	176 Dutch literate adult patients, diagnosed based on clinical evaluation and electrophysiology.
Interventions	Overnight splinting inmobilising the wrist in neutral position for at least six weeks versus standard open section of the carpal ligament.
Outcomes	Primary outcomes:

Gerritsen 2002

(*Continued*)

	(1) Relevant clinical improvement. (2) Number of nights that the patient woke due to the symptoms in a week. (3) Severity of the main complaint during the past week. Secondary outcomes: (1) Symptom severity and functional status scales. (2) Overall severity of CTS complaints scored by physiotherapist. (3) Neurophysiological parameters after 12 months. (4) Severity of pain, paraesthesia, and hypoesthesia both at night and during the day. All primary and two secondary outcomes were measured at 3, 6 and 12 months after randomisation.
Notes	Attempts were made to undertake a blind evaluation. The trial took place in the Netherlands.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Hui 2005

Methods	R = random computer-generated code. A research assistant not involved in the management of cases prepared and coded opaque envelopes containing the treatment allocation.
Participants	48 women and 2 men, with more than 3 months and less than one year duration of symptoms, diagnosed clinically and electhrophysiologically.
Interventions	Surgical decompression under local anaesthesia or steroid injection.
Outcomes	Primary outcome: Improvement in symptoms as measured by the global symptom score (GSS) 20 weeks after intervention. Secondary outcomes: (1) Electrophysiological measures (DML and sensory nerve conduction velocity) (2) grip strength measurements using a dynamometer.
Notes	Hong Kong, China

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Ly Pen 2005

Methods	R = random sequence generated by computer in blocks of 6 cases. Sealed envelopes containing the treatment assignments were provided by our biostatistics unit.
Participants	93 women and 8 men, 18 years old or older with symptoms of at least 3 months, unresponsive to a course of at least 2 weeks of nonsteroidal anti-inflammatory drugs and splinting. Clinically and electrophysiologically confirmed.
Interventions	Open surgery or steroid injection beneath the transverse carpal ligament from the ulnar side of the wrist.
Outcomes	Primary outcome: percentage of wrists reaching at least a 20% reduction in the VAS score for nocturnal paraesthesias at 3 months of follow up. Secondary outcomes: percentages of wrists with a 20% reduction in the VAS score for nocturnal paraesthesias at 6 and 12 months, a 20% response for pain and functional impairment, as well as a 50% and a 70% response in nocturnal paraesthesias, pain, and functional impairment.
Notes	Wrists rather than patients were used as the units for randomisation. Bilateral CTS were excluded from our analysis

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Sparapani 2006	Not randomised, as informed by the correponding author in a personal communication.

Characteristics of studies awaiting assessment *[ordered by study ID]*

Elwakil 2007

Methods	Not known
Participants	Not known
Interventions	Not known
Outcomes	Not known
Notes	Not known

Ucan 2006

Methods	Not known
Participants	Not known
Interventions	Not known
Outcomes	Not known
Notes	Not known

DATA AND ANALYSES

Comparison 1. Surgical versus non-surgical treatment - primary outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Improvement in clinical symptoms at three months	3	295	Risk Ratio (M-H, Fixed, 95% CI)	1.23 [1.04, 1.46]
2 Improvement in clinical symptoms at six months	2	245	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [1.02, 1.39]

Comparison 2. Surgical versus non-surgical treatment - secondary outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Clinical improvement at one year of follow-up	2	198	Risk Ratio (M-H, Fixed, 95% CI)	1.27 [1.05, 1.53]
2 Clinical improvement without including its relevance	1	50	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.43, 1.15]
2.1 Improvement in grip strength	1	50	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.43, 1.15]
3 Need for surgery or secondary surgery during follow-up	2	198	Risk Ratio (M-H, Fixed, 95% CI)	0.04 [0.01, 0.17]
4 Clinical improvement at less than three months	1	176	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.41, 0.98]
5 Complications of surgery and medical treatment	2	226	Risk Ratio (M-H, Fixed, 95% CI)	1.38 [1.08, 1.76]
6 Improvement in neurophysiological parameters	1	50	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [1.05, 1.97]
6.1 Change in amplitude of sensory potential	1	50	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [1.05, 1.97]

Analysis 1.1. Comparison 1 Surgical versus non-surgical treatment - primary outcomes, Outcome 1 Improvement in clinical symptoms at three months.

Review: Surgical versus non-surgical treatment for carpal tunnel syndrome

Comparison: 1 Surgical versus non-surgical treatment - primary outcomes

Outcome: 1 Improvement in clinical symptoms at three months

Study or subgroup	Surgical n/N	Non surgical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Gerritsen 2002	62/87	46/89		52.4 %	1.38 [1.08, 1.75]
Hui 2005	24/25	11/25		12.7 %	2.18 [1.39, 3.42]
Ly Pen 2005	21/36	29/33		34.9 %	0.66 [0.49, 0.90]
Total (95% CI)	**148**	**147**		**100.0 %**	**1.23 [1.04, 1.46]**

Total events: 107 (Surgical), 86 (Non surgical)

Heterogeneity: Chi² = 22.96, df = 2 (P = 0.00001); I² =91%

Test for overall effect: Z = 2.36 (P = 0.018)

Analysis 1.2. Comparison 1 Surgical versus non-surgical treatment - primary outcomes, Outcome 2 Improvement in clinical symptoms at six months.

Review: Surgical versus non-surgical treatment for carpal tunnel syndrome

Comparison: 1 Surgical versus non-surgical treatment - primary outcomes

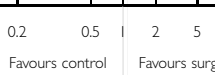
Outcome: 2 Improvement in clinical symptoms at six months

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Gerritsen 2002	72/87	57/89		69.2 %	1.29 [1.08, 1.55]
Ly Pen 2005	25/36	24/33		30.8 %	0.95 [0.71, 1.29]
Total (95% CI)	**123**	**122**		**100.0 %**	**1.19 [1.02, 1.39]**

Total events: 97 (Treatment), 81 (Control)

Heterogeneity: Chi² = 2.84, df = 1 (P = 0.09); I² =65%

Test for overall effect: Z = 2.17 (P = 0.030)



Analysis 2.1. Comparison 2 Surgical versus non-surgical treatment - secondary outcomes, Outcome 1 Clinical improvement at one year of follow-up.

Review: Surgical versus non-surgical treatment for carpal tunnel syndrome

Comparison: 2 Surgical versus non-surgical treatment - secondary outcomes

Outcome: 1 Clinical improvement at one year of follow-up

Study or subgroup	Surgery n/N	Splinting n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Garland 1964	10/11	2/11		3.3 %	5.00 [1.41, 17.76]
Gerritsen 2002	67/87	60/89		96.7 %	1.14 [0.95, 1.37]
Total (95% CI)	**98**	**100**		**100.0 %**	**1.27 [1.05, 1.53]**

Total events: 77 (Surgery), 62 (Splinting)

Heterogeneity: $Chi^2 = 5.73$, df = 1 (P = 0.02); $I^2 = 83\%$

Test for overall effect: Z = 2.47 (P = 0.013)

Analysis 2.2. Comparison 2 Surgical versus non-surgical treatment - secondary outcomes, Outcome 2 Clinical improvement without including its relevance.

Review: Surgical versus non-surgical treatment for carpal tunnel syndrome

Comparison: 2 Surgical versus non-surgical treatment - secondary outcomes

Outcome: 2 Clinical improvement without including its relevance

Study or subgroup	Surgery n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Improvement in grip strength					
Hui 2005	12/25	17/25		100.0 %	0.71 [0.43, 1.15]
Total (95% CI)	**25**	**25**		**100.0 %**	**0.71 [0.43, 1.15]**

Total events: 12 (Surgery), 17 (Control)

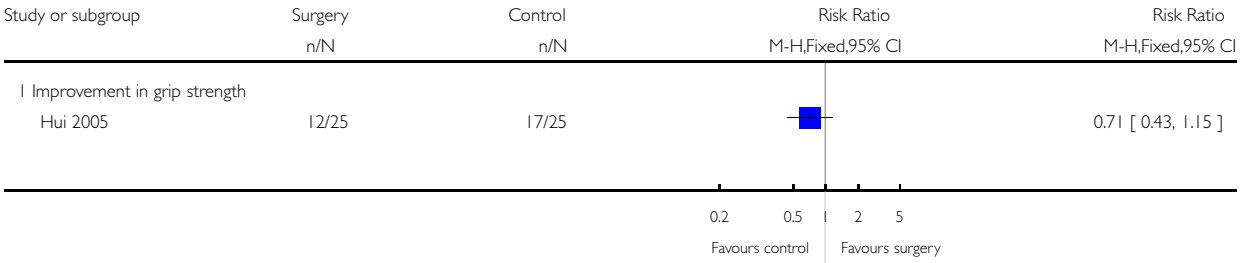
Heterogeneity: not applicable

Test for overall effect: Z = 1.40 (P = 0.16)

Review: Surgical versus non-surgical treatment for carpal tunnel syndrome

Comparison: 2 Surgical versus non-surgical treatment - secondary outcomes

Outcome: 2 Clinical improvement without including its relevance

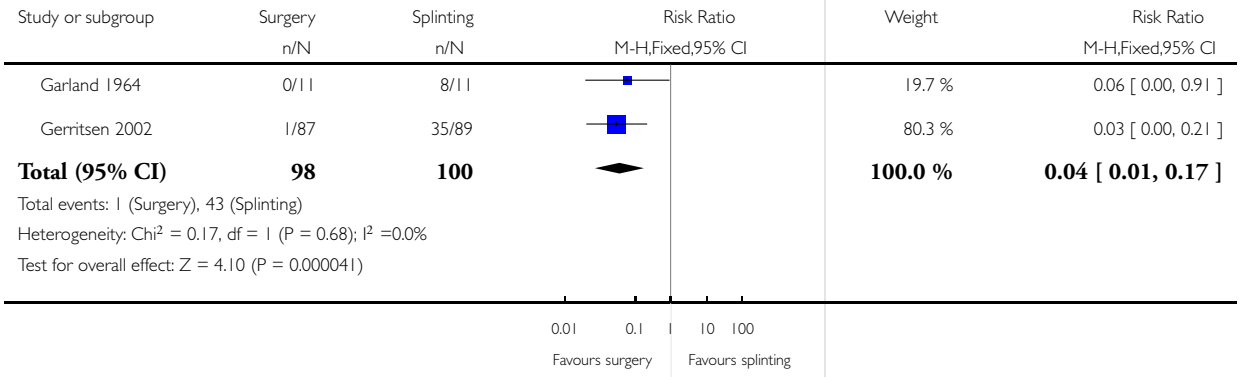


Analysis 2.3. Comparison 2 Surgical versus non-surgical treatment - secondary outcomes, Outcome 3 Need for surgery or secondary surgery during follow-up.

Review: Surgical versus non-surgical treatment for carpal tunnel syndrome

Comparison: 2 Surgical versus non-surgical treatment - secondary outcomes

Outcome: 3 Need for surgery or secondary surgery during follow-up



Analysis 2.4. Comparison 2 Surgical versus non-surgical treatment - secondary outcomes, Outcome 4 Clinical improvement at less than three months.

Review: Surgical versus non-surgical treatment for carpal tunnel syndrome

Comparison: 2 Surgical versus non-surgical treatment - secondary outcomes

Outcome: 4 Clinical improvement at less than three months

Study or subgroup	Surgical n/N	Non surgical n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Gerritsen 2002	23/87	37/89		100.0 %	0.64 [0.41, 0.98]
Total (95% CI)	**87**	**89**		**100.0 %**	**0.64 [0.41, 0.98]**
Total events: 23 (Surgical), 37 (Non surgical)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.07 (P = 0.038)					

Analysis 2.5. Comparison 2 Surgical versus non-surgical treatment - secondary outcomes, Outcome 5 Complications of surgery and medical treatment.

Review: Surgical versus non-surgical treatment for carpal tunnel syndrome

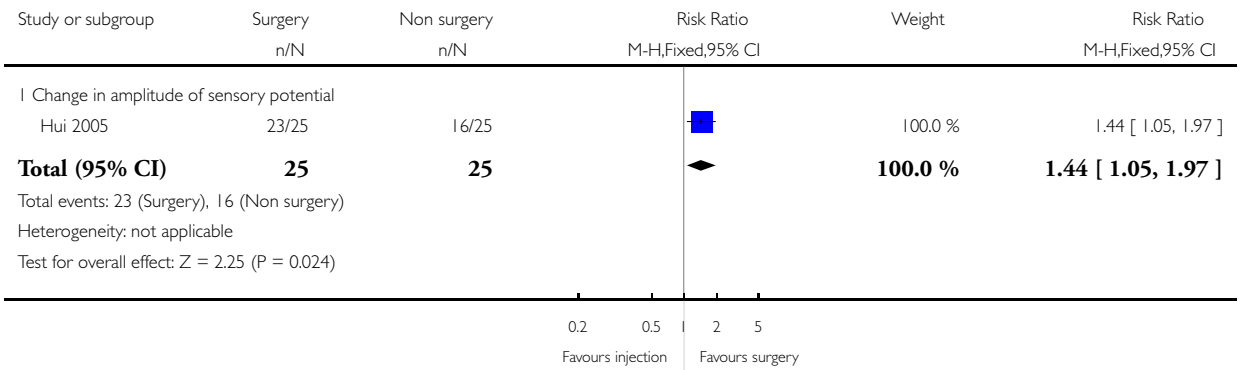
Comparison: 2 Surgical versus non-surgical treatment - secondary outcomes

Outcome: 5 Complications of surgery and medical treatment

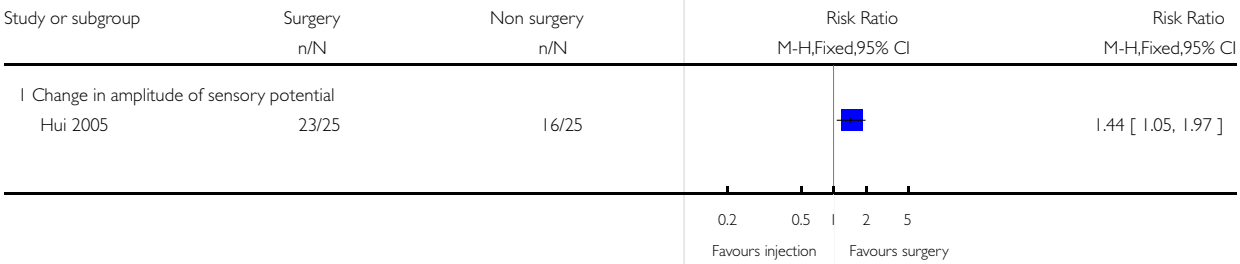
Study or subgroup	Surgery n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Gerritsen 2002	58/87	46/89		90.1 %	1.29 [1.00, 1.66]
Hui 2005	11/25	5/25		9.9 %	2.20 [0.89, 5.41]
Total (95% CI)	**112**	**114**		**100.0 %**	**1.38 [1.08, 1.76]**
Total events: 69 (Surgery), 51 (Control)					
Heterogeneity: Chi^2 = 1.31, df = 1 (P = 0.25); I^2 =24%					
Test for overall effect: Z = 2.58 (P = 0.010)					

Analysis 2.6. Comparison 2 Surgical versus non-surgical treatment - secondary outcomes, Outcome 6 Improvement in neurophysiological parameters.

Review: Surgical versus non-surgical treatment for carpal tunnel syndrome
Comparison: 2 Surgical versus non-surgical treatment - secondary outcomes
Outcome: 6 Improvement in neurophysiological parameters



Review: Surgical versus non-surgical treatment for carpal tunnel syndrome
Comparison: 2 Surgical versus non-surgical treatment - secondary outcomes
Outcome: 6 Improvement in neurophysiological parameters



APPENDICES

Appendix 1. MEDLINE search strategy

1 randomized controlled trial.pt.
2 controlled clinical trial.pt.
3 randomized controlled trials/
4 random allocation/
5 double-blind method/
6 single-blind method/
7 or/1-6
8 animals/ not humans/
9 7 not 8
10 clinical trial.pt.
11 exp clinical trials/

12 (clin$ adj25 trial$).ti,ab.
13 ((singl$ or doubl$ or tripl$ or trebl$) adj25 (blind$ or mask$)).ti,ab.
14 placebos/
15 placebo$.ti,ab.
16 random$.ti,ab.
17 research design/
18 or/10-17
19 18 not 8
20 19 not 9
21 comparative study/
22 exp evaluation studies/
23 follow up studies/
24 prospective studies/
25 (control$ or prospectiv$ or volunteer$).ti,ab.
26 or/21-25
27 26 not 8
28 27 not (9 or 20)
29 9 or 20 or 28
30 Carpal Tunnel Syndrome.mp. or Carpal Tunnel Syndrome/
31 (carp$ tunn$ or tunn$ syndrom$).mp
32 (nerve entrapment or nerve compression or entrapment neuropath$).mp
33 or/30-32
34 epineurotomy.mp.
35 reconstruct$.mp.
36 release.mp.
37 SURGERY/ or surgery.mp.
38 SURGICAL PROCEDURES, OPERATIVE/ or surgical.mp.
39 (splint or splints or splinting).mp.
40 exp Anti-Inflammatory Agents, Non-Steroidal/ or non-steroidal anti-inflammatory.mp.
41 NSAID$.mp.
42 ((corticosteroid$ or steroid$) and injection$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
43 diuretic$.mp. or exp DIURETICS/
44 or/34-43
45 33 and 44
46 29 and 45

Appendix 2. EMBASE strategy

1 Randomized Controlled Trial/
2 Clinical Trial/
3 Multicenter Study/
4 Controlled Study/
5 Crossover Procedure/
6 Double Blind Procedure/
7 Single Blind Procedure/
8 exp RANDOMIZATION/
9 Major Clinical Study/
10 PLACEBO/
11 Meta Analysis/
12 phase 2 clinical trial/ or phase 3 clinical trial/ or phase 4 clinical trial/
13 (clin$ adj25 trial$).tw.
14 ((singl$ or doubl$ or tripl$ or trebl$) adj25 (blind$ or mask$)).tw.
15 placebo$.tw.

16 random$.tw.
17 control$.tw.
18 (meta?analys$ or systematic review$).tw.
19 (cross?over or factorial or sham? or dummy).tw.
20 ABAB design$.tw.
21 or/1-20
22 human/
23 nonhuman/
24 22 or 23
25 21 not 24
26 21 and 22
27 25 or 26
28 carpal tunnel syndrome.mp. or Carpal Tunnel Syndrome/
29 (carp$ tunn$ or tunn$ syndrom$).mp.
30 (nerve entrapment or nerve compression or entrapment neuropath$).mp.
31 or/28-30
32 epineurotomy.mp. or carpal tunnel release/ or epineurotomy/
33 surgical approach/ or surgical technique/
34 (surgery or surgical or operation or reconstruct$).mp
35 33 or 34
36 (splint or splints or splinting).mp.
37 exp Nonsteroid Antiinflammatory Agent/ or non-steroid$ anti-inflammatory.mp.
38 NSAID$.mp.
39 ((corticosteroid$ or steroid$) and injection$).mp.
40 diuretic$.mp. or exp Diuretic Agent/
41 or/32-40
42 31 and 41
43 27 and 42

Appendix 3. LILACS strategy

median nerve entrapment OR carpal tunnel syndrome OR entrapment neuropathy [Words] and ((Pt randomized controlled trial OR Pt controlled clinical trial OR Mh randomized controlled trials OR Mh random allocation OR Mh double-blind method OR Mh single-blind method) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Pt clinical trial OR Ex E05.318.760.535$ OR (Tw clin$ AND (Tw trial$ OR Tw ensa$ OR Tw estud$ OR Tw experim$ OR Tw investiga$)) OR ((Tw singl$ OR Tw simple$ OR Tw doubl$ OR Tw doble$ OR Tw duplo$ OR Tw trebl$ OR Tw trip$) AND (Tw blind$ OR Tw cego$ OR Tw ciego$ OR Tw mask$ OR Tw mascar$)) OR Mh placebos OR Tw placebo$ OR (Tw random$ OR Tw randon$ OR Tw casual$ OR Tw acaso$ OR Tw azar OR Tw aleator$) OR Mh research design) AND NOT (Ct animal AND NOT (Ct human and Ct animal)) OR (Ct comparative study OR Ex E05.337$ OR Mh follow-up
studies OR Mh prospective studies OR Tw control$ OR Tw prospectiv$ OR Tw volunt$ OR Tw volunteer$) AND NOT (Ct animal AND NOT (Ct human and Ct animal))) [Words] and epineurotomy OR carpal tunnel release OR epineurotomy OR surg$ OR operation OR reconstruct$ OR splint$ OR non-steroid$ anti-inflammatory OR NSAID OR ((corticosteroid$ OR
steroid$) AND injection$) OR diuretic$ [Words]

WHAT'S NEW

Last assessed as up-to-date: 23 January 2008

Date	Event	Description
14 May 2008	New search has been performed	The review was updated to incorporate two new trials in January 2008.
14 May 2008	New citation required and conclusions have changed	The review was updated to incorporate two new trials in January 2008 resulting in a revision to the review conclusions.

HISTORY

Protocol first published: Issue 2, 1999

Review first published: Issue 2, 2002

Date	Event	Description
13 May 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Two authors (RS and RV) read the papers independently and agreed on inclusion. The data were extracted independently by three reviewers (RV, RS and JGC) using a structured sheet. The papers were discussed by three reviewers to clarify the statistical method used and the number of patients originally allocated to the different treatments. The review was written by all four reviewers.

DECLARATIONS OF INTEREST

None declared.

INDEX TERMS

Medical Subject Headings (MeSH)

Carpal Tunnel Syndrome [surgery; *therapy]; Randomized Controlled Trials as Topic; Splints

MeSH check words

Humans