Comparison of surgical decompression and local steroid injection in the treatment of carpal tunnel syndrome: 2-year clinical results from a randomized trial

Domingo Ly-Pen1, José-Luis Andréu2, Isabel Millán3, Gema de Blas4 and Alberto Sánchez-Olaso5

Abstract

Objective. To compare the efficacy of surgical decompression vs local steroid injection in the treatment of idiopathic CTS.

Methods. This is an open, prospective, randomized clinical trial. We studied the effects of surgical decompression vs local steroid injection in 163 wrists with a clinical diagnosis and neurophysiological confirmation of CTS, with an extended follow-up of 2 years. The primary end point was the percentage of wrists that reached a ≥20% improvement in the visual analogue scale score for nocturnal paraesthesia. Statistical analysis was done by Student’s t-test for continuous variables and by chi-square test for categorical variables. Analyses were performed on an intent-to-treat basis. P < 0.05 were considered statistically significant.

Results. Both treatment groups had comparable severity of CTS at baseline. Eighty wrists were randomly assigned to surgical decompression and 83 wrists to local steroid injection. Fifty-five wrists in the surgery group and 48 wrists in the injection group completed the 2-year follow-up. In the intent-to-treat analysis, at 2-year follow-up, 60% of the wrists in the injection group vs 69% in the surgery group reached a 20% response for nocturnal paraesthesia (P < 0.001).

Conclusion. Our findings suggest that both local steroid injection and surgical decompression are effective treatments in alleviating symptoms in primary CTS at 2-year follow-up. Surgery has an additional benefit in the 2-year follow-up, although clinical relevance of those differences remains to be defined.

Trial Registration: Current Controlled Trials, www.controlled-trials.com, ISRCTN26264638.

Key words: carpal tunnel syndrome, surgery, local steroid injection, randomized clinical trial.

Introduction

CTS is the most common entrapment neuropathy [1]. Clinically, CTS is characterized by signs and symptoms of irritation of the median nerve where it passes under the transverse carpal ligament at the wrist. Affected patients complain of numbness and pain in the hand and their symptoms typically worsen during nocturnal rest.

There are worthy clinical guidelines about the treatment of CTS [2, 3]. There is a trend to use conservative treatments in the less symptomatic cases, beginning with splinting [4]. Although there is no evidence for their usefulness, many physicians add NSAIDs [1, 5]. When splinting plus NSAID have failed, the second step is local steroid injection [1, 6]. Injection of CS has been shown to be superior to placebo in CTS [7, 8], and ~75% of patients experience improvement in symptoms after
a local injection of CSs [7, 9]. Surgical treatment is widely preferred over conservative therapies for very symptomatic and prolonged CTS, loss of sensibility, thenar weakness or atrophy, or severe involvement in nerve conduction studies [1, 6]. Unfortunately, there is no published evidence about the optimal treatment method for every subtype of CTS, such as mild vs severe disease or the presence of clinically evident motor impairment, with or without neurophysiological confirmation [10].

In a previous paper, we presented the results of the first year follow-up, comparing the effects of surgery vs injections in the treatment of CTS [11]; we demonstrated that injections were as safe and effective as surgery in idiopathic CTS at 1-year follow-up. The original study has been extended one more year because there is a clinical impression that injections had a greater relapse of symptoms than surgery [12]. This also happened in our previous paper, as the study advanced in time [13].

Patients and methods

Study design

This was a 1-year, prospective, randomized, open, comparative clinical trial of local steroid injection vs surgical decompression for new-onset CTS, conducted between October 1998 and May 2001. We have decided to prolong the original study one more year, following patients until May 2002. The Ethics Committee of Hospital Ramón y Cajal approved the study, and it was performed in accordance with the ethical principles of the Declaration of Helsinki. All patients provided written informed consent before study enrolment.

Treatment assignments were randomly generated by computer in blocks of six cases. In patients with bilateral CTS, treatment assignments were made for individual wrists. Sealed envelopes containing the treatment assignments were provided by our biostatistics unit. Immediately after patient enrolment, the envelope containing the treatment assignment for each wrist was opened, and the specific treatment was assigned. An intent-to-treat analysis was performed according to the number of wrists randomly assigned to surgery or local steroid injection.

Patients

Patients referred from primary care were included if they were >18 years, with symptoms suggesting CTS for at least 3 months, with an inadequate response to a course of splinting and NSAIDs for at least 2 weeks. All patients were evaluated by the same investigator (D.L.-P.) in a primary care setting. After undergoing a complete clinical history and physical examination, patients with a clinical diagnosis of CTS (pain, tingling, burning or numbness, or some combination of these symptoms, in the fingers in the distribution of the median nerve that may radiate to the forearm [1]) were invited to participate in the study, and informed consent was requested. Electrodiagnostic testing of both the median and ulnar nerves of the affected side were done by the same investigator (G.db.). CTS was confirmed according to Kimura’s criteria [14]. Exclusion criteria were thenar atrophy, previous carpal tunnel release surgery, previous local injection, pregnancy, diabetes mellitus, hypothyroidism, inflammatory arthropathy, polyneuropathy or simultaneous affection of the ulnar nerve in neurophysiological testing.

Treatment

All surgical procedures were performed on an outpatient basis by the same investigator (A.S.-O.) using a limited palmar incision technique, as previously described [15–17]. Local steroid injections were performed by the same investigator (D.L.-P.) using a standard technique [1, 16], with paramethasone acetonide, 20 mg in 1 ml. Treated wrists were evaluated 14 days after the initial treatment. In the operated wrists, the objective of this visit was to examine the evolution of the scar. In the injected wrists, the protocol allowed a second (and last) injection if nocturnal paraesthesias had not completely disappeared, with a score of 0 on the visual analogue scale (VAS). Thirteen wrists required one injection, and 69 wrists required two injections.

End points

At baseline, 3-, 6-, 12- and 24-month follow-up, patients used a 100-mm VAS (0 = no symptoms and 100 = the most intense symptoms) to assess their level of nocturnal parasthesias in the area of the distribution of the median nerve, their level of diurnal pain and their overall level of self-perceived functional impairment. At the time the study was initiated, the Disabilities of the Arm, Shoulder and Hand (DASH) Questionnaire [19] had not been validated in the Spanish population [20].

As for other rheumatic conditions, we assumed that a 20% improvement over baseline values would represent the minimum requirement for considering the therapeutic response to be clinically meaningful [21]. Since patients are more concerned with nocturnal symptoms than with daytime pain or functional impairment, the primary end point was the percentage of wrists reaching at least a 20% reduction in the VAS score for nocturnal parasthesias. Secondary end points were the percentages of wrists with a 20% reduction in the VAS score for pain and functional impairment, as well as a 50 and a 70% response in nocturnal parasthesias, pain and functional impairment. Treatment failure was defined as one of the following two features: absence of at least a 20% improvement in VAS scores over baseline scores for at least one of the three symptom dimensions at the 3-month visit, or reappearance or worsening of symptoms between visits at an intensity that represented <20% improvement from baseline. In wrists with treatment failure, an alternative therapy was decided on a clinical basis. Alternative therapy consisted of wide-incision surgical decompression in patients who had undergone limited-incision surgery and limited palmar-incision surgery in the patients who had received steroid injection. These wrists were considered study dropouts, and data from further follow-up visits were excluded from the study.
Statistical analysis

The sample size was calculated to achieve an 80% power to detect a difference of 20 units in the percentage of wrists reaching a 20% response in VAS scores for nocturnal paraesthesias between groups, assuming 70% of responders in the less favourable group, at a 5% \( \alpha \) level. The calculated sample size was 72 wrists per group. Percentages of wrists reaching 20, 50 and 70% improvement in VAS scores for nocturnal paraesthesias, pain and functional impairment were determined by intent-to-treat analysis. Categorical variables were compared by chi-square test, calculating the relative risk and the 95% CI, and by Fisher’s exact test. We also analysed the data according to the number of wrists that completed the study. The results of continuous variables were expressed as the mean (S.D.). For statistical analyses, Student’s \( t \)-test and the Mann–Whitney non-parametric test were used for comparisons between groups. During follow-up, VAS scores for nocturnal paraesthesias, pain and functional impairment were compared by repeated measures analysis of variance. All statistical tests were two-sided.

Results

Characteristics of the study population

One hundred and sixty-three wrists of 101 patients (93 women and 8 men) were randomized. Eighty wrists were assigned to surgery and 83 wrists to steroid injection. The groups were comparable in terms of symptom duration, age, sex and VAS scores for the three dimensions of symptoms (Table 1). Fifty-six patients underwent surgery; 24 of them had CTS in both wrists. Forty-nine patients received an injection; 34 of them had CTS in both wrists. Sixty-nine of the 82 injected wrists (84%) required two injections, according to the study protocol.

Fig. 1 shows the flow chart of the study. Twenty-five wrists in the surgery group did not complete the 24-month follow-up because of treatment failure (9 wrists), rejection of surgery after randomization (11 wrists) or moving out of town (5 wrists). In the injection arm, 35 wrists did not complete the 24-month follow-up because of treatment failure (26 wrists), rejection of local injection after randomization (1 wrist), Colles fracture (2 wrists) or moving out of town (6 wrists).

Efficacy

Intention-to-treat analysis

Fig. 2 shows the percentages of wrists that reached 20, 50 and 70% improvement in VAS scores for nocturnal paraesthesias at 3-, 6-, 12- and 24-month follow-up. Table 2 shows the percentages of wrists that reached 20, 50 and 70% response in each of the three symptom domains. With regard to nocturnal paraesthesias at 3-months follow-up, more wrists in the injection group than in the surgery group achieved a 20% response (94 vs 75%, respectively; \( P = 0.001 \)). This advantage vanished during the follow-up (Table 2). In fact, at 24-months follow-up, 60.2% of wrists in the injection group and 68.8% in the surgery group achieved a 20% response in nocturnal paraesthesias (\( P = 0.256 \)).

Results for the other two symptom domains (diurnal pain and self-perceived functional impairment) were similar, with differences at the 3-month follow-up favouring injection in 20, 50 and 70% responses (Table 2). In contrast, at the 24-month follow-up, surgery was more effective than injection in those achieving 70% improvement in functional impairment (60 vs 44.6% of responders in the surgery and injection groups, respectively; \( P = 0.049 \)) (Table 2).

Per-protocol analysis

Fig. 3 shows the mean VAS scores for the three symptom domains at baseline and 3-, 6-, 12- and 24-months follow-up of patients who completed the follow-up visits. Both procedures were highly effective in improving the three domains of symptoms. In essence, data were similar to those found in the intent-to-treat analysis. Among completers, local injection provided better results than surgery at the 3-month follow-up visit. The mean (s.d.) VAS scores for nocturnal paraesthesias at 3 months were 7.98 (17.38) in the injection group and 15.55 (25.37) in the surgery group (\( P = 0.034 \)). In contrast, at the 24-month follow-up, surgery was more effective than local injection for this symptom dimension, with mean VAS score of 8.81 (13.95) in the injection group vs 1.29 (4.51) in the surgery group (\( P < 0.001 \)).

With regard to diurnal pain, at the 24-month follow-up, surgery was as effective as local injection, with a mean VAS score of 3.04 (6.54) in the injection group vs 2.02 (7.26) in the surgery group (\( P = 0.19 \)). In contrast, surgery was more effective than injection as far as self-perceived functional impairment is concerned, with a mean VAS score of 6.21 (8.81) in the injection group vs 2.02 (7.23) in the surgery group (\( P = 0.008 \)).
Discussion

Our results show that, although both local steroid injection and surgical decompression are very effective therapies in alleviating symptoms in primary CTS, surgery is slightly superior to injection at 24-month follow-up. There is generally a lack of rigorous scientific support for non-surgical treatments in CTS [10, 22]. Whereas most studies evaluating local injection have been retrospective or uncontrolled, two systematic reviews of randomized controlled trials [23–25] concluded that local CS injection provides greater clinical improvement at 1 month compared...
with placebo. On the other side, surgical treatment is usually considered the definitive treatment of CTS [1, 10]. This is the first randomized controlled clinical trial that compares the two most common therapies for CTS: local injection of steroids and surgical decompression, and this is also the study with the longest follow-up, up to 2 years. In Hui’s study [26], 50 patients with clinically and electrophysiologically confirmed CTS were compared: 25 randomized to surgery vs 25 patients randomized to one single steroid injection. At 20-week follow-up, the surgery group had better symptomatic outcome, but not better grip strength.

In our previous study [11] at 1-year follow-up, we showed that the two therapies, injections and surgery, were very effective. Injection got better results than surgery at 3-month follow-up in terms of the three symptom domains. At 6 and 12 months, there were no statistically significant differences between these two treatments. At 6 and 12 months, surgery seemed to provide slightly better results than injection, but this difference did not reach statistical significance in our intent-to-treat analysis. Furthermore, as shown in the flow chart, the longer the time from injection to follow-up assessment, the greater the number of treatment failures in the injection group.

There are several differences between the studies of Hui et al. [26] and Ly-Pen et al. [11] that could explain this disparity of results [27]. In our study, patients were recruited from primary care, and in Hui’s trial, patients were recruited from neurology and rheumatology clinics. In our study, analysis was performed on an intent-to-treat basis, and rejection of treatment after randomization was considered as clinical failure. This happened in 11 wrists of the surgery group and in only 1 wrist of the injection group. In Hui’s study, none of the 50 patients included rejected the randomized treatment. Another critical difference was that, in our study, >80% of wrists required two injections, whereas only one injection was allowed in Hui’s study. The optimal number of injections per year and the time between them have not been studied. Interestingly, in a randomized double-blind controlled trial in CTS, Wong et al. [28] found no significant differences in electrophysiological and functional outcomes among 40 patients randomized to a single vs double steroid injections, 2 months apart. Nonetheless, neither the primary outcomes (VASs vs Global Symptom Score) nor the interval between injections (2 weeks vs 2 months) was the same in both the studies.

In the 2-year follow-up, the impression we got in our first description, that the longer the time from injection to follow-up assessment, the greater the number of treatment failures in the injection group, is confirmed: 10 of 66 wrists (15.1%) of the injection group had to be sent to surgery because of symptomatic relapse. Only 2 of 57 wrists (3.5%) of the surgery group relapsed at the end of the first year.

This makes sense if we think about the pathogenesis of CTS and the effect of each treatment: injections and surgery. Primary CTS is due to compression of the median nerve within the carpal tunnel (CT), usually by its ceiling, the flexor retinaculum. Steroids could reverse some pathogenic mechanisms in CTS [29], like suppression of synovial swelling and/or vascular congestion, with a secondary relief of local ischaemia, resulting in a reduction of the pressure inside the CT [29]. Theoretically, steroid injection may only provide provisional relief as long as the mechanical restriction persists, while section of the flexor retinaculum should provide greater space for the contents of the CT, and consequently should resolve the problem.
Our study has some limitations. This is not a double-blind study, but we thought a sham surgical procedure would be unethical. An injection in one wrist could theoretically result in improvement in the opposite, surgically decompressed wrist because of the systemic absorption of the CS. An overweighting effect cannot be ruled out.

<table>
<thead>
<tr>
<th>TABLE 2 Percentage of wrists reaching a 20, 50 and 70% response in the three dimensions of symptoms in an intention-to-treat analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3 months</strong></td>
</tr>
<tr>
<td><strong>Response</strong></td>
</tr>
<tr>
<td>20% np-VAS</td>
</tr>
<tr>
<td>20% p-VAS</td>
</tr>
<tr>
<td>20% f-VAS</td>
</tr>
<tr>
<td>50% np-VAS</td>
</tr>
<tr>
<td>50% p-VAS</td>
</tr>
<tr>
<td>50% f-VAS</td>
</tr>
<tr>
<td>70% np-VAS</td>
</tr>
<tr>
<td>70% p-VAS</td>
</tr>
<tr>
<td>70% f-VAS</td>
</tr>
</tbody>
</table>

The analysis of the percentage of wrists reaching 20, 50 and 70%. np-VAS, p-VAS and f-VAS responses were done on the basis of the intention-to-treat principle. The comparison between categorical variables was evaluated by the chi-square test, calculating the RR and the 95% CI. S: surgery; I: injection.
excluded in the surgically decompressed wrist when the other wrist has been injected. If this is the case, an apparent superiority of surgical decompression could be a bias of the study design. However, statistical analysis of data from operated wrists with or without an injected opposite wrist did not show any relevant difference (data not shown).

Another potential limitation is that the outcome measurements used in our study have not been formally validated. As previously mentioned at the time, the study was initiated, the DASH Questionnaire [19] had not been validated in the Spanish population [20]. We decided to use three percentage levels of improvement in VAS scores (20, 50 and 70%) as end points since they are considered relevant for clinical trials in other rheumatic disorders [21]. We used VAS scores for the three main dimensions of CTS symptoms (nocturnal paraesthesias, pain and functional impairment), which cover a wide array of symptoms reported by patients with CTS. As far as clinical assessment is concerned, we think that our end points were sufficiently representative of the symptoms reported by CTS patients in daily clinical practice.

Although randomization based on wrists instead of patients could be faulted [30], CTS is frequently a bilateral condition, and our approach is consistent with the standards of care in clinical practice, which consists of treating both wrists in cases of bilateral CTS.

We also felt that by randomizing only the most symptomatic wrist in bilateral cases, we could have a biased selection: the results of the study would not represent the real severity of CTS in the general population. Instead, the results of the study would be distorted: it would transform CTS into a more severe disease than it really is. Furthermore, a post hoc analysis taking into account only the more symptomatic wrist in bilateral cases and a generalized estimating equation approach did not modify the conclusions of our study [11].

In summary, our findings suggest that both local steroid injection and surgical decompression are effective treatments in alleviating symptoms in primary CTS at 24-month follow-up. Surgery has an additional benefit in the 12- and 24-month follow-up. Although a bias of the study design. However, statistical analysis of data from operated wrists with or without an injected opposite wrist did not show any relevant difference (data not shown).

**Acknowledgements**
The authors are indebted to Evelyn K. Robertson for her careful English revision.

**Disclosure statement.** The authors have declared no conflicts of interest.

**References**