The effect of epineurotomy on the median nerve volume after the carpal tunnel release: a prospective randomised double-blind controlled trial

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Received: 17 January 2012 / Accepted: 23 April 2012 / Published online: 17 May 2012
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Abstract

Purpose The purpose of this study was to evaluate the effects of epineurotomy on the post-surgical median nerve volume and clinical outcomes in carpal tunnel syndrome (CTS) patients with a prominent nerve narrowing.

Methods This was a prospective, randomised, double-blind controlled trial. Patients ($n=50$) were randomised (1:1) to open-field surgical carpal tunnel release followed by a

longitudinal epineurotomy of the nerve (test), or to open-field release without epineurotomy (control).

Results The nerve volume was slightly larger in the test group 90 days post-surgery (by 10.5 %, $p=0.157$) but not 180 days post-surgery. No relevant electrophysiological or clinical difference between groups and no effect of the nerve volume was observed. The subjective pain reduction was slightly more prominent in the control group at 180 days. Larger post-surgical nerve volume was associated with lower pain, but only in the control group.

Conclusions Even in selected CTS patients, longitudinal epineurotomy confers no benefit regarding the nerve volume or clinical outcomes over a simple carpal tunnel release.

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Introduction

The carpal tunnel syndrome (CTS) is the most common canalicular syndrome in humans and compressive neuropathy of the median nerve within the tunnel is a common cause of hand disability [1, 2]. Surgical release of the tunnel reduces pressure, allows for restoration of the intraneuronal blood flow and physiological function, and is treatment of choice in persistent/progressive cases [3]. Open-field and endoscopic techniques do not seem to differ in efficacy and patient satisfaction [4]. However, the open-field approach allows for manipulations that could additionally improve the outcomes. Long-lasting nerve compression may result in fibrotic changes generating further mechanical pressure and narrowing of the nerve. In such cases, longitudinal epineurotomy of the nerve as described by Foulkes et al. [5] and Leinberry et al. [6] has been suggested [7, 8] as an option that could convey a greater pressure release, a more prominent nerve volume recovery and better outcomes.

Consequently, the method has been widely used [9]. However, randomised controlled trials failed to demonstrate additional benefits of epineurotomy on the electrophysiological and clinical outcomes [5, 6, 10]. A potential limitation of these trials [5, 6, 10] was that they were not restricted to patients with a clear-cut nerve fibrosis/narrowing. We aimed to evaluate the concept underlying the recommendation about the use of epineurotomy. Our trial assessed the effects of epineurotomy on the post-surgical nerve volume and related it to the electrophysiological and clinical outcomes specifically in patients with a prominent nerve narrowing.

Patients and methods

General design and ethics

This single-centre, prospective, randomised, double-blind controlled trial was approved by the local Ethics Committee. Patients were randomised (1:1) to undergo open-field release of the carpal tunnel followed by a longitudinal epineurotomy of the median nerve [5, 6] (test), or the open-field release without epineurotomy (control), and were assessed 90 and 180 days post-surgery.

Eligible patients

Included were consecutive adults (≥ 18 years of age) with symptoms of CTS that could not be managed by conservative means meeting the following criteria: (a) verified CTS [clinical signs/symptoms, electromyoneurographical (EMNG) evaluation (distal sensory latency >3.5 ms and/or distal motor

latency >4.5 ms)] [11, 12]; (b) informed consent; and (c) intra-surgically verified narrowing of the median nerve within the tunnel. This was performed by the operating surgeon based on the appearance of the nerve in the form of an hourglass. Pregnant women and patients with a previous surgery of the affected hand were not included.

Randomisation and blinding

A randomisation list (permuted block, four per block) was kept in a sealed envelope without access by the investigators included in any phase of the trial. Since the inclusion was finally verified intra-surgically, the person in charge was present in the operating room and disclosed the assigned treatment. Further measures ascertained double-blinding: (a) patients were blinded to the treatment, (b) all operations were performed by the same surgeon, whereas the post-surgical clinical evaluations were performed by independent investigators, (c) EMNG evaluations were performed by the same blinded neurologist, (d) radiological evaluations were performed by the same blinded radiologist, and (e) data analysis was blinded.

Study flow and patient evaluations

Before the surgery, patients underwent EMNG (15–30 days before), radiological and clinical evaluations (one to three days before), and the same assessments were repeated 90 and 180 days after the surgery (± 7 days) (Fig. 1).

Magnetic resonance imaging (MRI) was used to estimate the median nerve volume within the carpal tunnel based on measurements performed in T2 and T2* WFS slices (Hitachi Airis-II 0.3T apparatus) with patients lying in the

Fig. 1 Study and patient flow. *EMNG* electromyoneurography, *MRI* magnetic resonance imaging, *DSL* distal sensory latency, *DML* distal motor latency, *VAS* visual analogue scale

prone position, the hand extended overhead and placed in a neutral position within a coil designed for the wrist [13, 14]. Proximal and distal borders of the carpal tunnel were determined in the coronal plain [13], and four to nine axial sections, 3-mm wide, were performed (section width, W), depending on the carpal tunnel length. The image was enlarged and the median nerve was outlined to obtain the area of the axial section (mm^2). Each section was outlined three times and the mean value for each section was obtained (mean axial area, MAA, mm^2). The volume of each axial nerve section was determined from the section area and section width (MAA $\times$ W) and their summation yielded the total estimated nerve volume within the carpal tunnel. Since the number of individual axial sections varied, the mean value (total nerve volume/number of axial sections) was used for treatment comparisons.

Orthodromic EMNG (MEB 2000 apparatus, Nihon Kohden) of the median nerve was performed in order

to estimate distal motor and distal sensory latency (DML, DSL, respectively) [15]. Motor and sensory conduction velocity and myography of the thenar eminence were also performed in order to verify the diagnosis.

Clinical assessments were performed at least five days after the last analgesic dose and evaluated [16]: (a) spontaneous pain (10-point visual analogue scale [VAS], 0=no pain to 10=excruciating pain), (b) subjective hand functionality (10-point VAS, 0=no dysfunction to 10=completely dysfunctional), (c) thenar hypotrophy, (d) range of movements and provocations tests, and (e) grip strength (kg) (dynamometer, Collin-Rudolf instruments).

Surgical procedures and post-surgical care

Operations were performed by a standardised technique [16] under pneumatic tourniquet control and general anaesthesia. A “square-root”-shaped skin incision was made and the carpal ligament was dissected. The test

Table 1 Patient characteristics

Characteristics	Epineurotomy (test) (<i>n</i> =25)	No epineurotomy (control) (<i>n</i> =25)
Age at surgery (years)	49.8 $\pm$ 12.3	53.7 $\pm$ 10.7
Men	4 (16)	13 (52)
Profession requires grip strength	19 (76)	23 (92)
The affected hand is dominant	16 (64)	13 (52)
Symptom duration (months)	24 (15–75)	24 (7.5–40.5)
Overuse syndrome	24 (96)	24 (96)
Clinical measures - primary		
Pain (visual analogue scale score)	5 (1.0–6.5)	5 (4.0–7.0)
Grip strength (kg)	17 (7.0–24.0)	15 (10.3–19.0)
Clinical measures - other		
Paraesthesiae	24 (96)	25 (100)
Hand oedema	9 (36)	8 (32)
Thenar hypotrophy	7 (29)	5 (20)
Volar flexion (degrees)	60 (50–70)	60 (40–65)
Dorsal flexion (degrees)	55 (40–70)	50 (40–65)
Ulnar abduction (degrees)	35 (30–40)	31 (30–40)
Radial abduction (degrees)	20 (20–30)	20 (20–30)
Electroneuromyography		
Distal motor latency (DML) (ms)	6.0 (5.2–7.7)	5.4 (4.8–6.7)
Absence of motor conduction	1 (4)	2 (8)
Distal sensory latency (DSL) (ms)	0 (0–4.6) (<i>n</i> =24)	0 (0–3.7)
Absence of sensory conduction	13 (54) (<i>n</i> =24)	16 (64)
Magnetic resonance imaging		
Median nerve volume in the carpal tunnel (mm^3)	41.4 $\pm$ 11.8	45.8 $\pm$ 11.1 (<i>n</i> =24)
Median nerve enlarged as it enters the carpal tunnel	14 (56)	13 (54) (<i>n</i> =24)
Flattening of the median nerve within the carpal tunnel	25 (100)	25 (100)
Increased signal of the median nerve on T2-weighted image	16 (64)	10 (42)
Volar bulging of the flexor retinaculum	4 (16)	2 (8)

Data are given as mean $\pm$ SD, count (%) or median (quartiles), as appropriate

procedure included a longitudinal incision of the ulnar palmar epineurium of the median nerve extending throughout the carpal tunnel [5, 6]. The wound was irrigated with sterile saline and only the skin was sutured (*Nylon 4-0*). The wrist was immobilised in dorsal flexion (five to ten degrees) for ten days. After removal of the immobilisation and sutures, all patients underwent the same rehabilitation protocol (cryotherapy, exercises of hand mobility, grip strength and limb circulation). The test procedure (from placement to removal of the tourniquet) lasted seven to 25 minutes and the control procedure lasted seven to 12 minutes.

Outcomes

Primary outcome was post-surgical median nerve volume. The four secondary outcomes referred to electrophysiological and objective and subjective clinical status: (a) proportion of patients with normal (≤ 4.5 milliseconds) or improved DML (reduction of ≥ 0.5 milliseconds vs. the pre-surgical value or any measurable value in patients with a motor block before the surgery), (b) proportion of patients with normal (≤ 3.5 milliseconds) or improved

DSL (as for DML), (c) grip strength, (d) VAS score for pain. Complications were also recorded.

Sample size and power considerations

Sample size was determined with respect to the primary outcome. We defined a difference of 25 % in post-surgical nerve volume as potentially relevant. With two repeated measures and one two-level between factor (treatment groups), sample size of 23 patients per group yields 80 % power at a two-sided 0.05 alpha level to detect such a difference, assuming first-order autoregressive covariance structure, correlation between measurements on the same subject of 0.5 and relative standard deviation of a single observation of 35 % [17]. Consequently, 25 subjects per group were included.

Data analysis

Not all patients underwent all of the planned assessments considering the defined outcomes (Fig. 1). Since the intention was to test for inequality, primary analysis

Fig. 2 Median nerve volume within the carpal tunnel by treatment and visit (a) and absolute and relative adjusted mean differences between treatments (b). *ITT (LOCF)* intent-to-treat patients with last observation carried forward, *PP* per protocol patients

was based on the intent-to-treat principle (ITT) and included all patients with the respective assessment performed at least before the surgery with last observation carried forward (ITT-LOCF). The analysis was also performed considering patients who underwent the assessments at post-surgical visits per protocol (PP-as measured). Data were analysed by fitting linear or generalised linear mixed models. We used SAS 9.2 for Windows (SAS Inc., Cary, NC).

Results

Apart from a higher proportion of men in the epineurotomy (test) than in the non-epineurotomy (control) group, before the surgery the groups were fairly comparable regarding patient characteristics and specifically, the median nerve volume within the tunnel, electrophysiological findings, grip strength and subjective pain evaluation (Table 1).

In both groups, the nerve volume was higher 90 days post-surgery than before the surgery (Fig. 2a). With adjustment for the pre-surgery value, age, sex and whether the affected hand was a dominant one, the increase was

somewhat higher in the test group (mean 9.9 mm³ in the ITT and 10.5 mm³ in the PP set, $p<0.001$, respectively) than in the control group (7.2 mm³ in both ITT and PP sets, $p=0.002$). At 180 days, the volume increased further, and the adjusted difference vs. the pre-surgery value was somewhat lower in the test (mean 13.3 and 13.7 mm³ for ITT and PP data, respectively, $p<0.001$) than in the control group (mean 14.6 and 14.7 mm³ for ITT and PP data, respectively, $p<0.001$). Consequently, the adjusted mean difference between the test and control treatment for the overall post-surgery period was slightly but insignificantly in favour of the test treatment (relatively, by around 5.7 % larger volume in the ITT and by around 9.4 % in the PP data set) (Fig. 2b). The difference was the largest at 90 days when it attained borderline statistical significance in the PP data set (by around 14.5 % larger nerve volume, $p=0.056$), whereas there was practically no difference between the treatments at 180 days post surgery (Fig. 2b).

The proportion of patients with normal or improved DML, and less so the proportion of patients with normal/improved DSL, was considerably higher in both groups at 90 days post-surgery than before the surgery, and further increased at 180 days post-surgery (Fig. 3a,b).

Fig. 3 Secondary efficacy outcomes by treatment and visit. **a** Distal motor latency (DML). **b** Distal sensory latency (DSL). **c** Grip strength. **d** Pain by visual analogue scale (VAS). *ITT (LOCF)* intent-to-treat patients with last observation carried forward, *PP* per protocol patients

Fig. 4 Adjusted mean differences between the test and control treatment in visual analogue scale (VAS) score for pain. *ITT (LOCF)* intent-to-treat patients with last observation carried forward, *PP* per protocol patients

No trend of differences between the two treatments at any time post-surgery was observed. Also, when the post-surgical nerve volume was considered as a time-varying covariate, no indication of an effect on DML or DSL was observed.

In the test group, grip strength was practically identical at 90 and 180 days post-surgery vs. pre-surgery, whereas in the control group it decreased at 90 days and returned to pre-surgery values at 180 days post-surgery (Fig. 3c). The decrease in the control group at 90 days was statistically significant (adjusted difference around -3.8 kg, in both ITT and PP sets, $p=0.006$). Consequently, at 90 days post-surgery grip strength was higher in the test than in the control group with borderline statistical significance (adjusted mean difference around 3.3 kg, $p=0.083$ in the ITT set, around 3.2 kg, $p=0.091$ in the PP set), whereas no such trend was seen for the overall post-surgery period or at 180 days post-surgery. Also, no indication of an effect of the post-surgical nerve volume on the grip strength was observed.

The VAS score for pain greatly decreased post-surgery in both groups (Fig. 3d). The adjusted differences in VAS pain

score vs. pre-surgery were highly statistically significant ($p < 0.001$) in both groups at both follow-up visits, in both ITT and PP data sets. However, the VAS pain score reduction was somewhat lower in the test than in the control group (e.g., in the ITT data set, around 2.5 and 2.9 points at 90 and 180 days in the test group vs. around 3.6 and around 4.7 points in the control group). Consequently, in the ITT data set, considering the overall post-surgery period, VAS score for pain was higher in the test than in the control group with borderline statistical significance (adjusted mean difference around 1.0 point, $p=0.056$) (Fig. 4), and it was significantly higher at 180 days post-surgery (difference around 1.38 points, $p=0.017$) (Fig. 4). In the PP set, the difference at 180 days was borderline significant (around 0.97 points, $p=0.090$) (Fig. 4). When the post-surgical nerve volume was considered as a time-varying covariate and with adjustment for treatment, visit, age, sex, pre-surgery VAS score and whether the affected hand was a dominant one, larger volume was associated with a lower VAS pain score in both ITT and PP data sets (Fig. 5). In both sets, the volume/treatment interaction was statistically significant indicating different relationship between the post-surgical nerve volume and pain score in the two treatment groups; while in the test group there was no apparent association, in the control group higher volume was associated with lower pain (Fig. 5).

There were no complications during the study. All patients were satisfied with the functional and cosmetic outcomes.

Discussion

It has been suggested that in the CTS patients with a prominent narrowing of the median nerve longitudinal epineurotomy would obtain a greater pressure relief, better nerve volume recovery and better outcomes than a standard carpal ligament dissection [7, 8]. Several trials have failed to demonstrate clinical and electrophysiological advantages of the procedure, however they were not restricted to

Fig. 5 The effect of the post-surgical median nerve volume on the post-surgical visual analogue scale (VAS) score for pain, overall and in the test and the control groups. *ITT (LOCF)* intent-to-treat patients with last observation carried forward, *PP* per protocol patients

patients with a prominent nerve narrowing/fibrosis [5, 6, 10]. Our trial is the first in this specific (sub)population and the first to assess the underlying concept that in these patients the procedure allows for a better nerve volume recovery, and by doing so, better clinical outcomes. It is limited by a relatively small sample, but it was powered to detect a reasonably small difference (25 %) between the test (epineurotomy) and control (no epineurotomy) procedure regarding the nerve volume. On the other hand, randomisation and blinding have achieved a fair level of internal validity. Under these circumstances, we observed a somewhat greater nerve volume in the test than in the control group 90 days post-surgery, but not 180 days post-surgery. The difference was modest and the trial was not sufficiently powered to detect it as statistically significant. Still, as it was similar for the ITT (around 10.5 %) and PP data (around 14.5 %), it appears that epineurotomy does enable a somewhat more rapid recovery of the nerve volume than the standard procedure. However, we found no evidence to support the concept that a larger increase in the nerve volume *per se* should *a priori* be considered beneficial. Although the increase in the nerve volume paralleled the improvement in the electrophysiological outcomes, we found no indication of an independent association between the two. Consequently, and in line with the previous trials [5, 6, 10], we found no evidence of a beneficial effect of epineurotomy on electrophysiological outcomes. It should be noted that the implemented measures were rather crude due to the fact that, as expected, motor and particularly sensory conductivity blocks were common in this (sub) population of patients, but should be considered practically informative. Similarly, we found no indication of an effect of a larger nerve volume on the grip strength, and no relevant difference between the two treatments in this respect. On the other hand, larger post-surgical nerve volume was independently associated with a greater self-reported pain reduction. However, the effect was apparent only with the control procedure suggesting that epineurotomy *per se* might modify the relationship between the nerve volume and post-surgical pain. In accordance with this finding, the reduction in the VAS pain scores appeared somewhat more pronounced in the control group resulting in somewhat higher VAS pain scores in the test group 180 days after the surgery. Although the difference attained statistical significance in the ITT data set, it was small in size (around 1.38 points) and probably without any practical relevance.

In conclusion, in line with other reports [5, 6, 10], the results suggest that even in selected patients longitudinal epineurotomy of the median nerve does not confer any relevant electrophysiological or clinical benefit (nor harm), as compared to a simple dissection of the carpal ligament. Moreover, they question the concept that in these patients a benefit could/should be expected due to a more prominent

effect on the nerve volume restoration. Therefore, the simple release of the carpal tunnel should be considered the surgical method of choice for the treatment of CTS [18–22].

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Bilić R, Kolundžić R, Jelić M (2001) Overuse syndromes of the hand, forearm and the elbow. *Arh Hig Rada Toksikol* 52:403–414
2. Kanaan N, Sawaya RA (2001) Carpal tunnel syndrome: modern diagnostic and management techniques. *Br J Gen Pract* 51:311–314
3. Lowry WEJ, Follender AB (1988) Interfascicular neurolysis in the severe carpal tunnel syndrome. A prospective, randomized, double-blind, controlled study. *Clin Orthop* 227:251–254
4. Bande S, DeSmet L, Fabry G (1994) The results of carpal tunnel release: open versus endoscopic technique. *J Hand Surg* 19:14–17
5. Foulkes GD, Atkinson RE, Beuchel C, Doyle JR, Singer DI (1994) Outcome following epineurotomy in carpal tunnel syndrome: a prospective, randomized clinical trial. *J Hand Surg* 19:539–547
6. Leinberry CF, Hammond NL III, Siegfried JW (1997) The role of epineurotomy in the operative treatment of carpal tunnel syndrome. *J Bone Joint Surg* 79:555–557
7. Palazzi S, Palazzi JL (1980) Neurolysis in compressive neuropathies. *Int Surg* 65:509–514
8. Fissette J, Onkelinx A (1979) Treatment of carpal tunnel syndrome. Comparative study with and without epineurolysis. *Hand* 11:206–210
9. Duncan KH, Lewis RC Jr, Foreman KA, Nordyke MD (1987) Treatment of carpal tunnel syndrome by members of the American Society for Surgery of the Hand: results of a questionnaire. *J Hand Surg* 12:384–391
10. Blair WF, Goetz DD, Ross MA, Steyers CM, Chang P (1996) Carpal tunnel release with and without epineurotomy: a comparative prospective trial. *J Hand Surg* 21:655–661
11. Gelberman RH, Pfeffer GB, Galbraith RT, Szabo RM, Rydevik B, Dimick M (1987) Results of treatment of severe carpal-tunnel syndrome without internal neurolysis of the median nerve. *J Bone Joint Surg* 69:896–903
12. Rhoades CE, Mowery CA, Gelberman RH (1985) Results of internal neurolysis of the median nerve for severe carpal-tunnel syndrome. *J Bone Joint Surg* 67:253–256
13. Bower JA, Stanisiz GJ, Keir PJ (2006) An MRI evaluation of carpal tunnel dimensions in healthy wrists: implications for carpal tunnel syndrome. *Clin Biomech* 21:816–825
14. Monagle K, Dai G, Chu A, Burnham RS, Snyder RE (1999) Quantitative MR imaging of carpal tunnel syndrome. *Am J Roentgenol* 172:1581–1586
15. Jablecki CK, Andary MT, So YT, Wilkins DE, Williams FH (1993) Literature review of the usefulness of nerve conduction studies and electromyography for the evaluation of patients with carpal tunnel syndrome. *Muscle Nerve* 16:1392–1414
16. Bilić R, Kolundžić R, Trkulja V, Crnković T, Vuković A (2006) The carpal tunnel syndrome: medical and economic advantages of well-timed surgical treatment. *Lijec Vjesn* 128:143–149

17. Liu H, Wu T (2005) Sample size calculation and power analysis of time-averaged difference. *J Modern Applied Stat Methods* 4:434–445
18. Corradi M, Paganelli E, Pavesi G (1989) Internal neurolysis and flexor tenosynovectomy: adjuncts in the treatment of chronic median nerve compression at the wrist in hemodialysis patients. *Microsurgery* 10:248–250
19. Holmgren LH, Leszniewski W, Linden U, Rabow L, Thorling J (1985) Internal neurolysis or ligament division only in carpal tunnel syndrome-results of a randomized study. *Acta Neurochir* 74:118–121
20. Holmgren LH, Rabow L (1987) Internal neurolysis or ligament division only in carpal tunnel syndrome. II. A 3 year follow-up with an evaluation of various neurophysiological parameters for diagnosis. *Acta Neurochir* 87:44–47
21. Chen CH, Wu T, Sun JS, Lin WH, Chen CY (2012) Unusual causes of carpal tunnel syndrome: space occupying lesions. *J Hand Surg* 37:14–19
22. Pećina MM, Krmpotić-Nemanić J, Markiewicz AD (2001) Tunnel syndromes. *Peripheral nerve compression syndromes*, 3rd edn. CRC Press, Boca Raton, pp 125–139