Ultrasound in Med. & Biol., Vol. 37, No. 10, pp. 1603–1608, 2011

0301-5629/$ - see front matter

ELSEVIER

doi:10.1016/j.ultrasmedbio.2011.07.002

● *Original Contribution*

EXTRACORPOREAL SHOCK WAVE THERAPY IN PILLAR PAIN AFTER CARPAL TUNNEL RELEASE: A PRELIMINARY STUDY

PIETRO ROMEO,* M. CRISTINA D'AGOSTINO,† A. LAZZERINI,‡ and VALERIO C. SANSONE*

*Orthopaedic Department of the Università degli Studi di Milano, Istituto Ortopedico Galeazzi, Milano, Italy; †Extracorporeal Shock Wave Unit, Istituto Clinico Humanitas, Rozzano, Italy; and ‡Hand Surgery Unit, Istituto Clinico Humanitas, Rozzano, Italy

(*Received* 13 *December* 2010; *revised* 29 *June* 2011; *in final form* 5 *July* 2011)

Abstract—"Pillar pain" is a relatively frequent complication after surgical release of the median nerve at the wrist. Its etiology still remains unknown although several studies highlight a neurogenic inflammation as a possible cause. Pillar pain treatment usually includes rest, bracing and physiotherapy, although a significant number of patients still complain of painful symptoms two or even three years after surgery. The aim of this study was to investigate the efficacy of low-energy, flux density–focused extracorporeal shock wave therapy (ESWT) in the treatment of pillar pain. We treated 40 consecutive patients with ESWT who had pillar pain for at least six months after carpal tunnel release surgery, and to our knowledge, this is the first study that describes the use of ESWT for treating this condition. Our results show that in all of the treated patients, there was a marked improvement: the mean visual analogue scale (VAS) score decreased from 6.18 (±1.02) to 0.44 (±0.63) 120 d after treatment, and redness and swelling of the surgical scar had also decreased significantly. (E-mail: valerio.sansone@unimi.it) © **2011 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Pillar pain, Extracorporeal shock waves, Carpal tunnel syndrome.**

INTRODUCTION

Open surgical release of the transverse carpal ligament for treatment of carpal tunnel syndrome (CTS) is an highly successful procedure. Nevertheless, it can be associated with persistent postoperative deep-seated ache or pain referred to the thenar or hypothenar eminences, with scar tenderness, swelling and redness, which have been variously described as "pillar pain" (PP) or "scar discomfort" (Da Silva et al. 1996; Ludlow et al. 1997; Boya et al. 2008). Because of the variety of terms used to describe this painful condition, its prevalence is difficult to ascertain, varying from 19–61%, according to different authors (Ahcan et al. 2002; Akhtar et al. 2007). The etiology is uncertain, although in the literature, many possible causes have been invoked such as surgical factors (Trumble et al. 2002; Povlsen et al. 1997), ligamentous and muscular conditions (Hunter 1991), biomechanical imbalance (Brooks et al. 2003) and neurogenic inflammation (Monacelli et al. 2008; van de Beek et al. 2002).

Extracorporeal shockwave therapy (ESWT) has been successfully used in the treatment of several painful inflammatory soft tissue conditions (Ogden et al. 2001; Wang 2003). Experimental studies have shown that low energy flux density (EFD) levels (0.03 mJ/mm^2) of shockwaves are able to induce a significant increase in nitric oxide (NO) and a decrease in pro-inflammatory substances such as nuclear factor–kappa B (NF-κB) (Mariotto et al. 2005). In other experimental studies, a reduction of the number of cutaneous nerve fibers and the immunoreactivity to the calcitonin gene–related peptide (CGRP) has been observed in mice treated with low EFD (0.08 mJ/mm^2) shockwaves (Ohtori et al. 2001). This reduction in CGRP was also observed in dorsal root ganglion neurons of mice (Takahashi et al. 2003). CGRP is a neuropeptide similar to substance P that is released by the nociceptor type C nerve fibers and is able to induce vasodilation and neurogenic inflammation (Herbert and Holzer 2002). Low EFD levels (0.03 mJ/mm^2) were shown to not produce microcellular damage (Steinbach et al. 1993), whereas negative effects on cell permeability were observed with relatively high

Address correspondence to: Valerio C. Sansone, M.D., Orthopaedic Department, Università degli Studi di Milano, Istituto Ortopedico Galeazzi, Via Galeazzi 4, 20161 Milano, Italy. E-mail: valerio.sansone@unimi.it

EFD level shockwaves (0.12 mJ/mm^2; Steinbach et al. 1992). On the basis of these experimental observations, we hypothesized a therapeutic effect of low EFD level shockwaves on the neurogenic inflammation, which is suspected to be behind PP (Monacelli et al. 2008). The energy level of 0.03 mJ/mm^2 was chosen because it was the lowest energy setting available on our lithotripter. We decided to increase the number of shots to counterbalance the low energy level, a decision reinforced by the positive experience of other studies, which report a similar number of shocks (Rompe et al. 1996; Khon and Seil 2000). The aim of this study was to verify the efficacy of low EFD shockwaves in treating PP.

MATERIALS AND METHODS

Forty consecutive patients (37 females, 3 males; mean age 51 y) who had PP after median nerve release for CTS were enrolled for ESWT. Informed consent was obtained and the study was approved by the ethics committee at the hospital. All patients received the same surgical treatment through an open mini-invasive incision at the palmar crease of the wrist, followed by a complete release of the transverse carpal ligament (Fig. 1). The surgery was performed by a single surgeon. The average time after surgery was 223 d (min 178, max 284).

A diagnosis of PP was made on the basis of the results of three clinical tests performed by a single evaluator for all patients: hand grip (Yung et al. 2005), application of direct pressure on the thenar and hypothenar regions (Wilson 1994) and the so-called "table test" (Boya et al. 2008), where the patient places their hands on the edge of a table, leaning their weight on their hands. Inclusion criteria were persistent palmar pain for at least three months after surgery; visual analogue score (VAS) $\geq$5 points (rating scale where 0 = absence of pain and10 = severe pain); scar reddening; and local edema. The levels of scar redness and edema were classified as follows: 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Patients who had an infection at the site of treatment were excluded from the study.

VAS, scar redness and edema grading were clinically evaluated by a single evaluator pre-treatment at (T0) and post treatment at 40 d (T1) and 120 d (T2). The patients underwent three treatments of ESWT, performed at weekly intervals using an electromagnetic device (MODULITH, SLK, Storz Medical, Tägerwilen, Switzerland), with an average of 2800 shocks at very low EFD of 0.03 mJ/mm^2. The pulse repetition frequency was 4 Hz. At EFD of 0.03 mJ/mm^2, the focal volume dimensions of the acoustic pulse were 6.5 mm (fx and fy) and 75 mm (fz), whereas the peak positive pressure was 6.4 MPa and the negative pressure was −3.4 MPa. At −6 dB focus, the positive energy generated was 3.9 mJ, and the total energy was 5.8 mJ. The shockwave probe was placed directly on the area of subcutaneous swelling and skin redness, or otherwise if no redness or edema were present, in the area between the thenar and hypothenar eminences. The impulses were focused superficially under sonographic control because the aim of the therapy was to treat the deep scar tissue.

Before undergoing ESWT (at time T0) all patients were submitted to magnetic resonance (MR) examination. Edema in the deep granulation tissue at the site of the transverse carpal ligament section was considered evidence of an abnormal development of the scar tissue

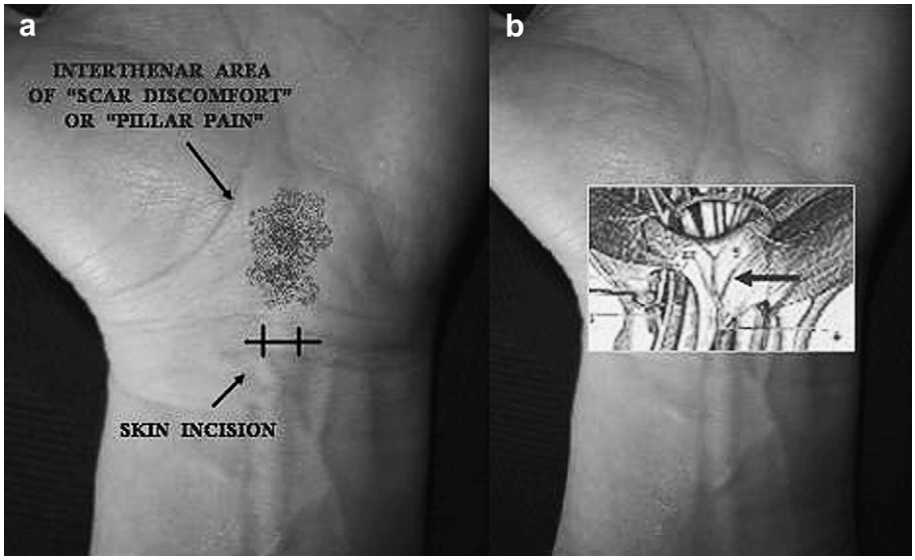

Fig. 1. (a) Patients report pain and swelling especially in the interthenar area. (b) Small unmyelinated fibers of the transverse carpal ligament.

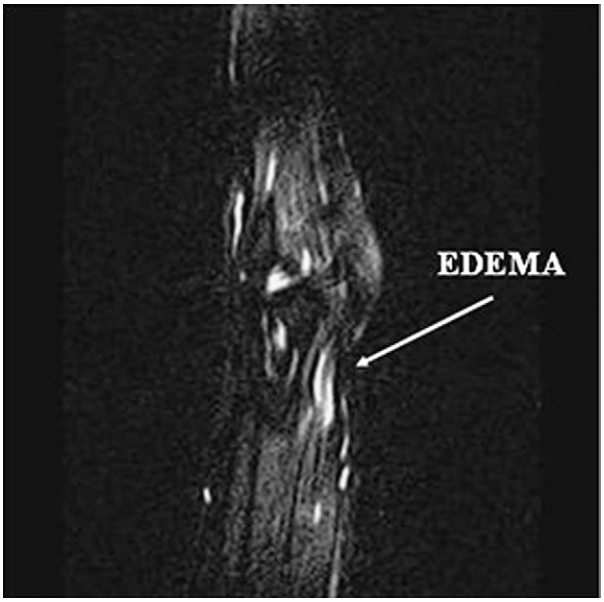

Fig. 2. NMR sagittal fat-suppressed F1 sequences. Edema in the deeper granulation tissue, at the site of transverse carpal ligament section.

(Fig. 2). Post-ESWT, MR assessments were available for four of the 40 patients, and these patients underwent additional MR scans at T1 and T2.

Statistical analysis of the results was performed to calculate mean values and standard deviation (SD) for the three variables (VAS, scar redness and edema), and the paired Student's *t*-test was used to analyze the difference of mean values and SD between the periods.

RESULTS

Our results showed a marked improvement in the individual scores of all patients at each follow-up time (see Table 1). At T2 (120 d post treatment), 60% of patients had no pain (*i.e.*, VAS score 0) and of the remaining 40%, no patient had a VAS score >2. At T2, 83% of patients had no skin redness and 100% had no edema.

The statistical analysis showed a significant difference in mean values ($p < 0.001$) regarding pain and scar redness between the T0 and T1 follow-ups, and between T1 and T2. Statistical analysis of the edema grades could only be performed for time periods T0 and T1, because by T2, the values were 0, but again, there was a significant reduction in values between T0 and T1 ($p < 0.001$).

We observed a positive correlation between pretreatment clinical findings and the inflammatory pattern of the MR images. MR examinations before treatment showed edema in the deep granulation tissue at the site of transverse carpal ligament in 36 patients (90%). The MR findings were not significant in the remaining four patients (10%), and these patients also had the lowest scores for pain, redness and scar edema. Other MR findings showed mild perineural edema in six patients (15%) and bone marrow edema of the carpal bones in two patients (5%).

The MR findings of the subgroup of four patients who underwent the additional MR follow-up showed an almost total disappearance of the inflammatory pattern imaging of edema in the deep scar tissue at T1 (1 mo post treatment). No local or general side effects were recorded during treatment or in the follow-up period.

DISCUSSION

Although open surgical treatment for CTS is normally successful (Gerritsen et al. 2001), a significant number of patients can develop postoperative PP. There is no agreement concerning the causes of this kind of scar discomfort, which occurs after surgical decompression of the median nerve in CTS. There are various hypotheses presented in the literature ranging from surgical causes, such as the skin incision, type of procedure (open or endoscopic), technical practice and surgeon's experience, to ligamentous and muscular causes. Biomechanical changes of the carpal arch width and of the flexor tendon pulley system have also been reported. Furthermore, recent studies hypothesize that the painful scar could be considered an expression of a reflex sympathetic dystrophy (van de Beek et al. 2002) owing to "neurogenic inflammation" (Monacelli et al. 2008), which probably includes different conditions characterized by a similar response to damage to nervous structures. According to some authors (Brooks et al. 2003; Biyani et al. 1996; Tomaino and Plakseychuk 1998; Wheatly et al. 1996), one mechanism could be the straining of the cutaneous nerve branches, caused by the incision of the "critical pillar rectangle" (Wilson 1994) or by the cutting of the small unmyelinated C nerve fiber in the superficial layer of the carpal ligament

Table 1. Interval scores for pain, skin redness and edema

Measurement	T0 (pre treatment)	T1 (40 d post treatment)	T2 (120 d post treatment)
VAS (pain)	6.18 ± 1.02 (Min. 4–Max. 8)	2.52 ± 1.07 (0–4.5)	0.44 ± 0.63 (0–2)
Skin redness	1.45 ± 0.75 (Min. 0–Max. 3)	0.75 ± 0.49 (0–2)	0.18 ± 0.3 (0–1)
Edema	1.38 ± 0.59 (Min. 0–Max. 2)	0.58 ± 0.5 (0–1)	0

The values are given as the mean and standard deviation with the range in parentheses.

(Da Silva et al. 1996). Other studies attribute a role to the entrapment of the sprouting nerve endings within the fibrous tissue of the scar (Biyani et al. 1996). Subjective and objective features seem to support the hypothesis of a neurogenic origin of PP in the context of a nonphysiological wound healing course. Wound healing is a complex process with specific cell–matrix interactions. Neuropeptides, released from the injured nerves, mediate the so-called "neurogenic inflammation phase," inducing vasodilatation mediated by cyclic-GMP and by endothelial NO (Karabucak et al. 2005). It has been shown that NO modulates cytokines and induces wound contraction in scar remodelling (Cobbold 2001). Inadequate NO substrate, or reduced NO substrate availability, appears to induce defective wound repair as in the case of hypertrophic scars (Peters et al. 2006; Schwentker and Billiar 2003). In these samples, a greater density of neuropeptides and nociceptive fibers has been observed when compared with normal scars (Crowe et al. 1994; Parkhouse et al. 1992). Cheloids and hypertrophic scars, which have an excess of collagen fibers and microvessels, may be considered a model of neurogenic inflammation.

An increase of neuropeptides, such as substance P, CGRP and also VEGF, EGF, TGFb1 and NGF, has been observed in both epidermis and dermis as a reaction of the sensory fibers to mechanical stress. According to some authors (Akaishi et al. 2008; Chin et al. 2009), the pathogenesis of neurogenic inflammation first involves the antidromic release of neuropeptides from sensory fiber endings. Neuropeptides may act as a chemo-attractive agent for Langherans cells, mast cells, endothelial cells, fibroblasts and immune cells (Chin et al. 2009; Lai et al. 2003). Also they influence antigen presentation, sensory neurotransmission, mast cell degradation, vasodilatation and vascular permeability, which collectively can cause neurogenic inflammation (Chin et al. 2009). This would justify the erythema, the edema and the hyperthermia of the skin. Recent studies highlight that persistent compression of a nerve, as in the case of CTS, causes a steady neuronal depolarization and consequently an irregular release of neuropeptides. The additional trauma of surgery would heighten the peripheral neurogenic inflammation (Monacelli et al. 2008). The severing of the C–nerve fibers in the superficial layer of the transverse carpal ligament could cause an up-regulation of neuropeptides (CRGP-SP) and a self-perpetuating, neurogenic inflammation, which in turn is responsible for a hypertrophic, immature and painful scar. One can observe that, although the surgical incision is situated at the palmar crease of the wrist, pain and swelling are found most commonly at the interthenar area, exactly where the surgeon cut the transverse carpal ligament (Fig. 1). This observation compares favorably with the findings of our study: the patients who showed an inflammatory pattern in their MR scans with edema in the deeper granulation tissue at the site of transverse carpal ligament also showed the highest clinical scores for pain, redness and scar edema before treatment.

Shockwaves have been shown to be an effective method of treating both acute and chronic soft tissue painful inflammations (Ogden et al. 2001; Wang 2003). Even if their mechanism of action is still being studied and is not yet completely understood, acoustic stimulation of living tissues seems to influence the complex NO pathway. This matrix–cell interaction, based on mechanotransduction, exerts an angiogenic and trophic effect and is able to modulate inflammation (Mariotto et al. 2005). In particular, the biphasic effect of the shockwaves (*i.e.*, the positive peak pressure followed by the negative cavitational effect) would induce structural modifications of the cell membrane. This implies the activation of free radicals and cytoplasmatic messengers. The outcome of these endocellular reactions, which are dose-dependent, is the production of several bioactive moleculae such as neoangiogenic factors (VEGF, eNOS) and cell proliferation factors (proliferating cell nuclear antigen).

NO may exert either an excitatory or an inhibitory effect on neuronal transmission (Riedel and Neeck 2001). On this basis, we considered the use of ESWT for treating PP. The standard therapy of scar discomfort after transverse carpal ligament release includes physiotherapy, bracing and rehabilitation, but results are inconclusive and pain is still relevant even several years after surgery. Povlsen et al. (1997) found PP in 41% of patients at one month, 25% at three months, 6% at 12 months and 6% at 36 months. Boya et al. (2008) reported that at 20.2 months' follow-up, >12.7% of patients still had PP. In our study, at 120 d after treatment, no patient had a VAS score >2 and 100% had no edema. The total disappearance of edema may be related to the mechanical effect of shockwaves on the extracellular matrix. The effects of shockwaves continue over an extended period of time after their application. Therefore, the continued presence of skin redness and subjective pain at 120 d could be connected to the level of neuropeptides, which, although low, would reduce further over time. Recently, a different treatment has been proposed, consisting of a series of at least six cutaneous and subcutaneous injections of mepivacaine 2%, twice weekly for three weeks (Monacelli et al. 2008). Six weeks after treatment, scar discomfort was still present in 25% of patients, and in 6.5% of patients after 18 weeks. Although it is difficult to compare our data with the aforementioned study because we used different evaluation criteria, our findings demonstrate a faster recovery from symptoms, with the additional benefit in this case that ESWT is a noninvasive treatment.

Statistical analysis revealed a highly significant improvement of VAS, edema and scar redness, not only

from pretreatment to final follow-up at T2, but also at the interim follow-up at 40 d (T1). There is controversy regarding the validity of the VAS scale, because absolute pain levels and changes in pain level over time are by nature subjective. However, it still remains the most widely adopted and validated system for evaluating chronic pain. Patients with PP often have difficulty describing precisely the painful symptoms, and therefore the VAS test with its simple linear scale was the best tool available to measure and compare the pain. Our findings would have had greater validity if a control group had been included in this study to highlight the speed of recovery after ESWT. However, looking at the literature and in our experience, conventional conservative treatment (*e.g.*, splinting, ultrasound, iontophoresis, laser therapy, *etc.*) usually gives inconclusive results and requires considerable time to evaluate the healing (Ludlow et al. 1997).

CONCLUSIONS

Our results seem to confirm the role of neurogenic inflammation in PP consequent to open carpal tunnel release. Even if PP resolves spontaneously, in many cases this may occur only after years rather than months, substantially reducing patient satisfaction with the original surgical treatment. In our study, ESWT proved to be a valid, safe and noninvasive tool that significantly reduced the recovery time from symptoms. However, it must be noted that this, although prospective, is a preliminary and noncontrolled study. Therefore, further studies are required to validate our findings.

REFERENCES

Ahcan U, Arnez ZM, Bajrović F, Zorman P. Surgical technique to reduce scar discomfort after carpal tunnel release. J Hand Surg (Am) 2002; 27:821–827.

Akaishi S, Ogawa R, Hyakusoku H. Keloid and hypertrophic scar: Neurogenic inflammation Hypotheses. Med Hypoth 2008;71:32–38.

Akhtar S, Sinha S, Bradley MJ, Burke FD, Wilgis SEF, Dubin NH. Difference in outcome following open carpal tunnel decompression performed by surgeon of different grade. Orthop Ann R Coll Surg Engl 2007;89:785–788.

Biyani A, Wolfe K, Simison AJ, Zakhour HD. Distribution of nerve fibres in the standard incision for carpal tunnel decompression. J Hand Surg (Am) 1996;21:855–857.

Boya H, Özcan Ö, Öztekn H. Long-term complications of open carpal tunnel release. Muscle Nerve 2008;38:1443–1446.

Brooks JJ, Schiller JR, Allen SD, Akelman E. Biomechanical and anatomical consequences of carpal tunnel release. Clin Biomech 2003;18:685–693.

Chin MS, Lancerotto L, Helm DL, Dastouri P, Prsa MJ, Ottensmeyer M, Akaishi S, Orgill D, Ogawa R. Analysis of neuropeptides in stretched skin. Plastic Reconstr Surg 2009;124:102–113.

Cobbold CA. The role of nitric oxide in the formation of keloid and hypertrophic lesions. Med Hypoth 2001;57:497–502.

Crowe R, Parkhouse N, McGrouther D, Burnstock G. Neuropeptide–containing nerves in painful hypertrophic human scar tissue. Br J Dermatol 1994;130:444–452.

Da Silva MF, Moore DC, Weiss AP, Akelman E, Sikirica M. Anatomy of the palmar cutaneous branch of the median nerve: Clinical significance. J Hand Surg (Am) 1996;21:639–643.

Gerritsen AA, Uitdehaag BM, van Geldere D, Scholten RJ, de Vet HC, Bouter LM. Systematic review of randomized clinical trials of surgical treatment for carpal tunnel syndrome. Br J Surg 2001;88: 1285–1295.

Herbert MK, Holzer P. Neurogenic inflammation II. Pathophysiology and clinical implications. Anasthesiol Intensivmed Notfallmed Schmerzther 2002;37:386–394.

Hunter JM. Recurrent carpal tunnel syndrome, epineural fibrous fixation, and traction neuropathy. Hand Clin 1991;7:491–504.

Karabucak B, Walsch H, Jou YT, Simchon S, Syngcuk K. The role of endothelial nitric oxide in the Substance P induced vasodilation in bovine dental pulp. J Endod 2005;31:733–736.

Kohn D, Seil R. Extracorporeal shock wave therapy in patients with tennis elbow and painful heel. Arch Orthop Trauma Surg 2000; 120:304–307.

Lai XN, Wang ZG, Zhu JM, Wang LL. Effect of substance P on gene expression of TGF beta–1 and its receptors in rats fibroblasts. Chin J Traumatol 2003;6:350–354.

Ludlow KS, Merla JL, Cox JA, Hurst LN. Pillar pain as a postoperative complication of carpal tunnel release: A review of the literature. J Hand Ther 1997;10:277–282.

Mariotto S, Cavalieri E, Amelio E, Ciampa AR, De Prati AC, Marlinghaus E, Russo S, Suzuki H. Extracorporeal shock waves: From lithotripsy to anti-inflammatory action by NO production. Nitric Oxide 2005;12:89–96.

Monacelli G, Rizzo MI, Spagnoli AM, Pardi M, Irace S. The pillar pain in the carpal tunnel's surgery. Neurogenic inflammation? A new therapeutic approach with local anaesthetic. J Neurosurg Sci 2008;52:11–15.

Ogden JA, Alvarez RG, Levitt R, Marlow M. Shock wave therapy (Orthotripsy) in musculoskeletal disorders. Clin Orthop Relat Res 2001;387:22–40.

Ohtori S, Inoue G, Mannoji C, Saisu T, Takahashi K, Mitsuhashi S, Wada Y, Takahashi K, Yamagata M, Moriya H. Shock waves application to rat skin induces degeneration and reinnervation of sensory nerve fibers. Neurosci Letter 2001;315:57–60.

Parkhouse N, Crowe R, McGrouther DA, Burnstock G. Painful hypertrophic scarring and neuropeptides. Lancet 1992;340:1410.

Peters EM, Ericson ME, Hosoi J, Seiffert K, Hordinsky MK, Ansel CJ, Paus R, Sholzen TE. Neuropeptide control mechanisms in cutaneous biology: Physiological and clinical significance. J Invest Dermatol 2006;126:1937–1947.

Povlsen B, Tegnell L, Revell M, Adolfsson L. Touch allodynia following endoscopic (single portal) or open decompression for carpal tunnel syndrome. J Hand Surg (Br) 1997;22:325–327.

Riedel W, Neeck G. Nociception, pain, and antinociception: Current concepts. Z Rheumatol 2001;60:404–415.

Rompe JD, Hopf C, Kullmer K. Low energy shock wave therapy on chronic tennis elbow. J Bone Joint Surg Br 1996;78-B:233–237.

Schwentker A, Billiar TR. Nitric oxide and wound repair. Surg Clin North Am 2003;83:521–530.

Steinbach P, Hofstaedter F, Nicolai H, Roessler W, Wieland W. Determination of the energy dependent extent of vascular damage caused by high energy shock waves in umbilical cord model. Urol Res 1993; 21:279–282.

Steinbach P, Hofstaedter F, Nicolai H, Roessler W, Wieland W. In vitro investigations on cellular damage induced by high energy shock waves. Ultrasound Med Biol 1992;18:691–699.

Takahashi N, Wada Y, Ohtori S, Saisu T, Moriya H. Application of shock waves to rat skin decreases calcitonin-related peptide immunoreactivity in dorsal root ganglion neurons. Aut Neurosci 2003;107:81–84.

Tomaino MM, Plakseychuk A. Identification and preservation of palmar cutaneous nerves during open carpal tunnel release. J Hand Surg (Br) 1998;23:607–608.

Trumble TE, Diao E, Abrams RA, Gilbert-Anderson MM. Single-portal endoscopic carpal tunnel release compared with open release: A prospective, randomized trial. J Bone Joint Surg (Am) 2002;84:1107–1115.

Van de Beek WJT, Schwartzman RJ, van Nes SI, Delhaas EM, van Hilten JJ. Diagnostic criteria used in studies of reflex sympathetic dystrophy. Neurology 2002;58:522–526.

Wang CJ. An overview of shock wave therapy in musculoskeletal disorders. Chang Gung Med J 2003;26:220–232.
Wheatly MJ, Hall JW, Faringer PD. Are the palmar cutaneous nerves safe during standard carpal tunnel release? Ann Plast Surg 1996; 37:251–253.
Wilson KM. Double incision open technique for carpal tunnel release: An alternative to endoscopic release. J Hand Surg (Am) 1994;19:907–912.
Yung PS, Hung LK, Tong CW, Ho PC. Carpal tunnel release with a limited palmar incision: Clinical results and pillar pain at 18 months follow-up. Hand Surg 2005;10:29–35.