



Recommendations for Neuropathic Pain Associated with Peripheral Nerve Entrapment or Injury

The Multidisciplinary Panel on Neuropathic Pain*

I. Introduction

Peripheral nerve injury is often associated with neuropathic pain symptoms, which are caused by trauma to the nerve or by nerve entrapment. These recommendations describe some of the more common causes of neuropathic pain due to peripheral nerve entrapment or injury. The recommendations are structured by nerve level as follows:

- Root level:
 - Cervical radiculopathy
 - Sciatica

- Peripheral nerve level:
 - Carpal tunnel syndrome
 - Cubital tunnel syndrome
 - Other sites

Treatment of neuropathic pain associated with nerve injury differs from other neuropathic pain conditions, such as postherpetic neuralgia, painful diabetic neuropathy and trigeminal neuralgia, as surgical decompression and nerve repair are often first-line treatment options rather than pharmacotherapy. In the presence of a definite mechanical compression, the primary goal is to achieve

* Panel members:

Chen Phoon Ping, MBBS, FANZCA, FFPANZCA, FHKCA, FHKAM, DipPainMgt

Consultant, Department of Anaesthesiology, Intensive Care and Operating Services, Alice Ho Miu Ling Nethersole Hospital, and Adjunct Associate Professor, The Chinese University of Hong Kong, Hong Kong SAR.

Josephine WY Ip, MBBS, MS, FRCS(Ed), FHKAM(Ortho), DipHandSurg(FESSH)

Chief, Division of Hand and Foot Surgery, Department of Orthopaedic Surgery, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR.

Joseph MK Lam, MBChB, FRCS(Edin), FCSHK, FHKAM(Surg)

Consultant Neurosurgeon and Adjunct Associate Professor, Division of Neurosurgery, Department of Surgery, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR.

Lee Tsun Woon, MBBS, FANZCA, FFPANZCA, FHKCA, FHKAM(Anaesthesiology), DipPainMgt

Chief of Service and Service Director (Clinical & Ambulatory Care), Department of Anaesthesia & Intensive Care, Tuen Mun Hospital, Hong Kong SAR.

Tsoi Tak Hong, MBBS, MRCP, FRCP(Edin), FRCP(Glas), FHKCP, FHKAM(Med)

Specialist in Neurology and Consultant Physician, Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR.

Wong Chun Por, MBBS, FHKAM(Med), FRCP(Lond), FRCP(Glas), FRCP(Edin), FHKCP

Chief of Service, Integrated Medicine Service, Consultant Geriatrician, and Head, Department of Geriatrics, Ruttonjee Hospital, Hong Kong SAR.

Lawrence KS Wong, MBBS, MD, MRCP, FHKAM(Med), FRCP

Associate Professor, Division of Neurology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR.

The Multidisciplinary Panel on Neuropathic Pain is supported by an educational grant from Pfizer Corporation Hong Kong Limited.

Table 1. Diagnosis, management and treatment of neuropathic pain associated with nerve injury/entrapment at the root level

| | Cervical radiculopathy | Sciatica |
|------------------|---|---|
| Diagnosis | <ul style="list-style-type: none"> • Cervical spine or neck x-ray • CT or MRI scan of the spine • Electrophysiological studies* • Myelogram (not commonly used) | <ul style="list-style-type: none"> • Physical examination (muscle weakness, poor reflexes, reduced sensation) • MRI • Electrophysiological studies* • Myelogram (largely replaced by MRI) |
| Treatment | <p><i>Conservative treatment:</i></p> <ul style="list-style-type: none"> • Cervical collar • NSAIDs • Physiotherapy/neck care exercises • For neuropathic pain symptoms, anticonvulsants or antidepressants may be effective <p><i>Surgical interventions:</i></p> <ul style="list-style-type: none"> • Decompression of the spinal cord or nerve root | <p><i>Conservative treatment:</i></p> <ul style="list-style-type: none"> • Physiotherapy • Oral NSAIDs • PENS/TENS <p><i>Nonsurgical treatment:</i></p> <ul style="list-style-type: none"> • Gabapentin • Epidural corticosteroid injection • Chemonucleolysis <p><i>Surgical interventions:</i></p> <ul style="list-style-type: none"> • Discectomy |

*Electrophysiological studies are recommended in cases where clinical diagnosis is not certain.
 CT = computed tomography; MRI = magnetic resonance imaging; NSAIDs = nonsteroidal anti-inflammatory drugs;
 PENS = percutaneous electrical nerve stimulation; TENS = transcutaneous electrical nerve stimulation

surgical decompression of the nerve. However, conservative treatment and pharmacotherapy tend to be more effective when magnetic resonance imaging (MRI) shows little bulging of the affected nerve. Neuropathic pain sometimes persists following surgical decompression or repair of compressed or damaged nerves. In these cases, pharmacotherapy is an appropriate treatment option.

II. Neuropathic Pain Associated With Nerve Injury at the Root Level

Cervical Radiculopathy

Cervical radiculopathy is a common symptom in patients with cervical spondylosis. Cervical spondylosis is a degenerative condition of the cervical vertebrae, intervertebral discs and surrounding ligaments. While cervical spondylosis may occur in people with a previous neck injury, the main risk

factor is ageing. Symptoms typically include neck pain, pain and paraesthesia radiating down the arms, dizziness, headache, progressive neck stiffness and progressive weakness of the upper limb. Cervical spondylosis is a common cause of dizziness in people older than 65 years,¹ caused when the vertebral arteries are compressed by osteophytes. Paraesthesia or numbness in the distribution of a cervical spinal nerve is characteristic of radiculopathy. Cervical radiculopathy is commonly the result of nerve compression at the root caused by a bulging intervertebral disc, osteophytes or a hypertrophic facet joint. Recommendations for diagnosis and management of cervical radiculopathy associated with spondylosis are summarized in Table 1.

Diagnosis

Patients with cervical spondylosis usually complain of progressive neck

pain and often have limited head and neck movement. Pain or paraesthesia occurs when the spinal cord or nerve roots are compressed. Key investigations in the diagnosis of cervical spondylosis include²: (1) cervical spine or neck x-ray: degenerative changes consistent with cervical spondylosis should be present, including narrowing of the disc space by osteophytes; (2) computed tomography (CT) or MRI scan of the spine: to confirm that the nerve root or spinal cord are compressed; (3) neurophysiological studies: nerve conduction testing and electromyography (EMG) to measure skeletal muscle activity; and (4) myelogram: this invasive technique can confirm the extent of nerve damage, but is not commonly used.

Treatment

Treatment of cervical spondylosis may include short-term use of a cervical collar during the acute phase, nonsteroidal anti-inflammatory drugs (NSAIDs), neck care exercises, postural training and intermittent cervical traction. While many cases of cervical spondylosis respond to conservative treatment, patients with cervical radiculopathy may require surgical decompression of the nerve root. Patients with painful cervical radiculopathy and neuropathic pain symptoms may improve with pharmacotherapy.

Surgery is indicated when other treatments have failed. The main aim of surgery in cervical spondylosis patients is decompression of the spinal cord or nerve root. However, surgical interventions are associated with complications (1% to 8% of patients), including death (up to 1.8%).³ Complications resulting from damage to the spinal cord include tetraplegia, and those resulting from

damage to the nerve root include muscle weakness. Patients presenting with pain only are the most difficult group to treat; surgery tends to be more beneficial in patients with severe neurological deficits.

Surgical decompression of the nerve root is often achieved via an anterior approach with removal of the intervertebral disc and osteophyte, or a posterior approach with laminectomy. A recent Cochrane review on the role of surgery in cervical spondylotic radiculomyelopathy identified two controlled trials involving 130 patients.³ The most common surgical interventions were via an anterior cervical approach with spinal fusion. Patients receiving surgery via a posterior approach underwent laminectomy. Control interventions included physiotherapy, hard or soft cervical collar, anti-inflammatory drugs, intermittent bed rest and prevention of vigorous activities. Surgery patients had greater improvements in pain, weakness and sensory loss in the short term than control patients. However, after 1 to 2 years' follow-up, there were no significant differences observed between groups. The authors concluded that there was inadequate data with which to determine whether surgical interventions were superior to more conservative therapy.³ A minimally invasive posterior approach for foraminotomy without laminectomy may also be an appropriate surgical intervention in selected cases.⁴

Lumbar Level: Sciatica

Sciatica is a common cause of low back pain, occurring when the sciatic nerve or lumbar root nerves are compressed. It is often accompanied by pain radiating from the back into the buttock and, sometimes, down the entire leg.

Symptoms of sciatica include changes in sensation in the calf muscle and feet, numbness, pain (which may be severe) and paraesthesia. Patients with sciatica may also have weakness in the knee or foot and difficulty walking. Recommendations for diagnosis and management of sciatica are summarized in Table 1.

Diagnosis

Patients with sciatica may have weak muscles in the affected myotome, sensory deficit in the affected dermatome, a positive straight-leg raising test and reduced reflexes. Pinprick sensation may be reduced on the affected side. Some of the more common tests to diagnose sciatica include: (1) MRI to determine the location of disc herniation; (2) electrophysiological studies measuring sensory nerve conduction velocity, motor nerve conduction velocity, waveform and amplitude, if there is doubt about the diagnosis; and (3) myelogram, which is invasive and has largely been replaced by MRI.

Treatment

Conservative treatment for sciatica is often appropriate as sciatica can resolve with time. Conservative procedures and surgical intervention often show similar outcomes in the long term. Maintaining mobility is important; bed rest has minimal effectiveness in reducing pain and symptoms associated with sciatica.⁵ Physiotherapy, including hot packs, manipulation and intermittent pelvic traction, may be beneficial. Oral NSAIDs may help improve sciatic pain and symptoms.⁶

Epidural corticosteroid injections provide short-term symptom relief; however, it is less clear whether these benefits are maintained in the long term.^{7,8} Few side effects have

been reported with epidural corticosteroid injections.^{7,8} Percutaneous and transcutaneous electrical nerve stimulation (PENS/TENS) has also been shown to provide short-term relief and improve function in sciatica patients.⁹ Longer-term use of such nerve stimulation tends not to provide additional benefits.

Other treatments for sciatica include chemonucleolysis, which can provide long-term relief.⁸ Although there are few adverse effects associated with this technique (<0.1% of cases), those that do occur may be serious (e.g. anaphylaxis, infection and neurological deficit). A surgical intervention for sciatica is discectomy, which has a high success rate (80%-96%), but is only slightly better in the long term than nonsurgical management.⁸

A recent study demonstrated that gabapentin was effective in patients with chronic radiculopathy (L4-5 and/or L5-S1 bulging and/or protrusion).¹⁰ This study randomized 50 patients to gabapentin (up to 3,600 mg daily in 3 divided doses) or placebo for an 8-week trial period, with gabapentin-treated patients achieving significant improvements in pain at rest and other clinical parameters.¹⁰

III. Neuropathic Pain Associated With Nerve Injury at the Peripheral Level

Median Nerve: Carpal Tunnel Syndrome

Entrapment or compression of the median nerve can cause carpal tunnel syndrome, anterior interosseous syndrome and pronator teres syndrome. The focus in these recommendations will be on carpal tunnel syndrome, as it is the most common of these conditions.

Carpal tunnel syndrome results from compression of the median nerve in the carpal tunnel. Symptoms mostly affect the hand, but can also radiate to the elbow. They include paraesthesia, tingling, numbness (particularly at night-time), clumsiness and weakness.

The most common cause of carpal tunnel syndrome is repetitive stress injury or overuse syndrome. It is the most common nerve entrapment neuropathy, and usually affects women. Carpal tunnel syndrome may be bilateral, but often affects the dominant hand first. Predisposing factors include repetitive finger or wrist movements, such as typing or household chores, and a congenital narrowing of the carpal tunnel.

Other than repetitive injury, carpal tunnel syndrome may also be caused by local and systemic conditions. Local causes include trauma, synovitis, arthritis, vascular injury and local tumour. Systemic causes include endocrine or metabolic disorders, infection, collagen disease and chronic renal failure. Recommendations for diagnosis and management of carpal tunnel syndrome are summarized in Table 2.

Diagnosis

Clinical signs and symptoms of carpal tunnel syndrome include: (1) wasting of the thenar muscles; (2) weak thumb abduction and opposition; (3) decreased pinprick sensation in the radial 3½ fingers, with sensation intact in the palm; and (4) positive Tinel sign and Phalen’s test.

Investigations for diagnosis of carpal tunnel syndrome include: (1) tests to determine whether there is a systemic cause, e.g. renal function test, blood sugar levels, thyroid function test; (2) x-ray of the hand and wrist with a carpal tunnel view;

and (3) electrophysiological studies, including sensory nerve conduction velocity, motor nerve conduction velocity, waveform and amplitude, with or without electromyography of the thenar muscle.

Treatment

Conservative Treatment: Conservative treatment of carpal tunnel syndrome includes splinting the wrist in a neutral position, physiotherapy (e.g. ultrasound), oral steroids, local steroid injections and diuretics. Oral steroid use may result in systemic side effects, including fluid retention and hypertension, and weight distribution and menstrual cycle disturbances, which limit use in some patients. While local steroid injections are often effective, complications include injury to the tendon or nerve, and infection. Acupuncture, including laser acupuncture, may

also reduce pain.

A randomized, double-blind study was performed to compare ultrasound with a ‘sham’ ultrasound procedure in patients with mild-to-moderate idiopathic carpal tunnel syndrome.¹¹ Patients receiving ultrasound demonstrated significantly greater improvements in subjective symptoms and electroneurographic variables. These effects were maintained for the 6-month follow-up period.

Patients should also be advised on good ergonomics and the importance of taking rest at intervals to minimize repetitive injury. Tasks that require hand or wrist movements should be reduced, such as hand-washing clothes or twisting a mop. Surgical treatment is indicated when conservative treatment has failed, there is motor involvement or the patient has severe numbness.

Table 2. Diagnosis, management and treatment of neuropathic pain associated with peripheral nerve injury/entrapment

| | Carpal tunnel syndrome | Cubital tunnel syndrome |
|------------------|--|--|
| Diagnosis | <ul style="list-style-type: none"> Physical examination (muscle wasting, decreased sensation, Tinel sign, Phalen’s test) Laboratory tests to ascertain potential systemic cause Hand and wrist x-ray, with carpal tunnel view Electrophysiological studies* | <ul style="list-style-type: none"> Physical examination (including claw hand deformity, weakness, reduced sensation) X-ray of elbow, with a cubital tunnel view Electrophysiological studies* |
| Treatment | <p><i>Conservative treatment:</i></p> <ul style="list-style-type: none"> Physiotherapy Wrist splinting Oral steroids and local steroid injections Diuretics <p><i>Surgical interventions:</i></p> <ul style="list-style-type: none"> Carpal tunnel release (open or endoscopic) | <p><i>Conservative treatment:</i></p> <ul style="list-style-type: none"> Does not have a significant role in treatment <p><i>Surgical interventions:</i></p> <ul style="list-style-type: none"> Simple neurolysis Anterior transposition of the ulnar nerve Medial epicondylectomy of the distal humerus |

*Electrophysiological studies are recommended in cases where clinical diagnosis is not certain.

Drug Treatment: Drug therapy for mild-to-moderate carpal tunnel syndrome includes NSAIDs, diuretics and oral steroids. A randomized, placebo-controlled trial of these agents found that 4 weeks' treatment with oral corticosteroids resulted in greater improvements in global symptom score than the other medications.¹² A more recent study found that patients treated with oral prednisolone for 2 or 4 weeks had similar overall improvements.¹³ The study concluded that short-term, low-dose oral steroids are effective for carpal tunnel syndrome.

Local steroid injection is also an effective therapy for carpal tunnel syndrome. Injection with methylprednisolone proximal to the carpal tunnel improved symptoms at 1 month in 77% of patients in the intervention group (n=30) compared with 20% of patients in the control group (n=30).¹⁴ After 12 months' follow-up, about half the patients were still receiving benefit from the single injection of methylprednisolone. Comparison of local versus systemic corticosteroids revealed that a single local injection of methylprednisolone was superior to a 10-day course of oral prednisolone.¹⁵

Surgical Intervention: Surgical treatment is indicated when conservative treatment has failed, there is motor involvement, or the patient has severe numbness. Some patients may experience recurrence of symptoms following surgery, so in selected cases further surgery is indicated. Until recently the standard procedure for carpal tunnel syndrome was open carpal tunnel release (OCTR) via a long, palmar curvilinear incision. The less invasive technique of endoscopic carpal tunnel release (ECTR) has now been developed. A

systematic review of randomized clinical trials of surgical treatment for carpal tunnel syndrome concluded that standard OCTR remains the preferred surgical procedure.¹⁶ Symptom relief with other procedures was similar to OCTR. Evidence on whether ECTR allows an earlier return to work and/or normal activities was variable. OCTR is also technically less demanding, so is associated with a lower risk of complications.¹⁶ ECTR is now a common procedure, but is more expensive than OCTR and is associated with more severe complications, such as nerve injury.

Ulnar Nerve: Cubital Tunnel Syndrome

Cubital tunnel syndrome arises from injury or compression of the ulnar nerve at the elbow. This results in pain, paraesthesia and numbness along the ulnar aspect of the hand. The patient may complain that their hand has become clumsy and weak.

The key causes of cubital tunnel syndrome include tardive ulnar palsy due to an old fracture, deformity of the elbow, rheumatoid arthritis, osteoarthritis, a ganglion or lipoma, a subluxing ulnar nerve and a supracondylar spur. Recommendations for diagnosis and management of cubital tunnel syndrome are summarized in Table 2.

Diagnosis

The clinical signs of cubital tunnel syndrome include: (1) claw hand deformity; (2) weak flexor carpi ulnaris and flexor digitorum profundus to the ring finger and little finger; (3) atrophy of intrinsic muscles, except for the thenar muscles and two radial lumbrical muscles; (4) weak finger abduction; (5) positive Froment sign; (6) reduced pinprick

sensation in the ulnar 1½ fingers and corresponding area of the palm and dorsum; and (7) positive Tinel sign at the level of the median epicondyle.

Tests to confirm the diagnosis of cubital tunnel syndrome include: (1) x-ray of the elbow, with a cubital tunnel view; and (2) electrophysiological studies measuring sensory nerve conduction velocity, motor nerve conduction velocity, waveform and amplitude, with or without electromyography of the muscle supplied by the ulnar nerve.

Treatment

Conservative treatment does not have a great role in treatment of ulnar neuropathy at the elbow; a release operation is frequently required. The most common surgical interventions are: (1) simple neurolysis; (2) anterior transposition of the ulnar nerve; and (3) medial epicondylectomy of the distal humerus.

Other Sites

Tarsal tunnel syndrome results from compression of the posterior tibial nerve or plantar nerves in the tarsal tunnel. Symptoms include pain, numbness and tingling paraesthesia in the sole of the foot. Poor-fitting footwear, post-traumatic fibrosis, tendon sheath cysts or tenosynovitis, ganglia, rheumatoid arthritis, hypothyroidism, acromegaly or a thickening of the flexor retinaculum can cause tarsal tunnel syndrome.

Treatment of tarsal tunnel syndrome where there is no motor deficit includes drug therapy, such as NSAIDs and anticonvulsants, e.g. gabapentin. If symptoms persist, surgical intervention to release the nerve is required.

References

1. Colledge NR, Barr-Hamilton RM, Lewis SJ,

- Sellar RJ, Wilson JA. Evaluation of investigations to diagnose the cause of dizziness in elderly people: a community based controlled study. *BMJ* 1996;313:788-792.
2. MEDLINEplus Medical Encyclopedia Web site. Cervical spondylosis. Available at: <http://www.nlm.nih.gov/medlineplus/ency/article/000436.htm>. Accessed June 2, 2004.
3. Fouyas IP, Statham PFX, Sandercock PAG. Cochrane review on the role of surgery in cervical spondylotic radiculomyelopathy. *Spine* 2002;27:736-747.
4. Witzmann A, Hejazi N, Krasznai L. Posterior cervical foraminotomy. A follow-up study of 67 surgically treated patients with compressive radiculopathy. *Neurosurg Rev* 2000;23:213-217.
5. Vroomen PCAJ, de Krom MCTFM, Wilmink JT, Kester ADM, Knottnerus JA. Lack of effectiveness of bed rest for sciatica. *N Engl J Med* 1999;340:418-423.
6. Dreiser RL, Le Parc LM, Vélicitat P, Llleu PL. Oral meloxicam is effective in acute sciatica: two randomized, double-blind trials versus placebo or diclofenac. *Inflamm Res* 2001;50(Suppl 1):S17-S23.
7. Carette S, Leclaire R, Marcoux S, et al. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. *N Engl J Med* 1997;336:1634-1640.
8. Samanta A, Beardsley J. Sciatica: which intervention? *BMJ* 1999;319:302-303.
9. Ghoname EA, White PF, Ahmed HE, et al. Percutaneous electrical nerve stimulation: An alternative to TENS in the management of sciatica. *Pain* 1999;83:193-199.
10. Yildirim K, SiSecioglu M, Karatay, et al. The effectiveness of gabapentin in patients with chronic radiculopathy. *Pain Clinic* 2003;15:213-218.
11. Ebenbichler GR, Resch KL, Nicolakis P, et al. Ultrasound treatment for treating the carpal tunnel syndrome: Randomized "sham" controlled trial. *BMJ* 1998;316:731-735.
12. Chang MH, Chiang HT, Lee SS, Ger LP, Lo YK. Oral drug of choice in carpal tunnel syndrome. *Neurology* 1998;51:390-393.
13. Chang MH, Ger LP, Hsieh PF, Huang SY. A randomized clinical trial of oral steroids in the treatment of carpal tunnel syndrome: A long-term follow-up. *J Neurol Neurosurg Psychiatry* 2002;73:710-714.
14. Dammers JWJH, Veering MM, Vermeulen M. Injection with methylprednisolone proximal to the carpal tunnel: Randomized double blind trial. *BMJ* 1999;319:884-886.
15. Wong SM, Hui ACF, Tang A, et al. Local vs systemic corticosteroids in the treatment of carpal tunnel syndrome. *Neurology* 2001;56:1565-1567.
16. Gerritsen AAM, Uitdehaag BMJ, van Geldere D, et al. Systematic review of randomized clinical trials of surgical treatment for carpal tunnel syndrome. *Br J Surg* 2001;88:1285-1295.