

Does Surgical Decompression for Symptomatic DPN Have a Place?

BY AARON I. VINIK, MD, PhD



A number of evidence-based reviews for the treatment of diabetic neuropathies (DPN) have been published recently.¹ Based on an all published material, the American Diabetes Association (ADA) has reviewed the evidence for treatment of autonomic neuropathy² as well as somatic

neuropathy³ and arrived at a position statement on recommendations for the treatment of diabetic neuropathies.⁴ The position statement supports an active pursuit of identifying patients with entrapment syndromes, and if proven, recommends medical or surgical therapy as deemed appropriate.

Surgical decompression of multiple nerves, however, is being used to treat common or *garden-variety* symptomatic DPN based on the hypothesis that diabetic nerves are more vulnerable to compressive injury and subject to a *double crush*. The first crush is metabolic, microvascular and autoimmune abnormalities and neurotrophin deficiency; the second is entrapment which occurs in confined compartments such as the tarsal tunnel. While this may be true, there are data to the contrary, ie that diabetic axons are really resistant to compression.⁵ Up to one-third of patients with diabetes have an entrapment syndrome, thus, it has become mandatory to distinguish entrapment from DPN, as well as its superimposition upon DPN.⁶ See related articles on pages 20 through 25.

Notwithstanding this difficulty in identifying appropriate patients for decompression, more than 240 surgeons in 41 states in the United States and 15 countries have been trained to perform decompression surgery. As recently reported (Chaudry et al *Neurology*, 2006, 66: 1805-1808), as of January 2006, 1,280, surgeries on 990 patients by 34 surgeons have been registered (www.neuropathyregistry.com). A literature search using Medline, EMBASE and PUBMED found 75 articles using the key words, diabetes mellitus, diabetic neuropathy and decompression and two more since this search. Only 11 articles dealt with decompressive surgery for DPN and only one that was prospective. In this study of 20 patients, 22% had nerve compression, 56% had DPN and 22% had DPN without nerve compression — the details of which were not provided. As indicated it can be difficult to discern but is mandatory if we are to pick those people who might be appropriate for surgical decompression.

Unfortunately, despite the contention that a positive

Tinel's sign identifies those people with entrapment superimposed upon DPN, there is a very high false positive and false negative rate. In a study of 1,528 hands diagnosed as having carpal tunnel syndrome, Nora et al⁷ reported that a Tinel's sign was positive in only 34% and the Phalen's sign in 56%. Much more distressing was the fact that there was a high false positive rate in patients with fibromyalgia and tendonitis. Thus, one would have to exercise extreme caution in using this sign as a determinant of candidates for surgical decompression.

Clearly the gold standard for diagnosis of nerve entrapment is nerve conduction demonstrating a block at the site which should be mandatory. In a study of 4,600 patients using the NC Stat system of measurement of nerve conduction at sites of possible entrapment it was extremely rare to find patients with entrapment of the tibial nerve that could be distinguished from DPN. In the reported results it has furthermore been impossible to determine if the improvements in nerve conduction have been in patients with DPN or those that actually have an entrapment. While the ADA strongly supports seeking out patients with entrapments who might benefit from decompression, it does not condone surgery in the absence of demonstrable entrapment.⁴

In the 10 nonblinded case series, eight of 10 studies reported pain relief by the operating surgeon 80% to 92% of the time even on the operating table recovering from the anesthetic. Patients have been evaluated pre and postoperatively for two-point discrimination using the Pressure-specified Sensory Device (Sensory Management Services, LLC, Baltimore) and reported an improvement in 67% to 89% of those studied who had the combined procedure of decompression of the posterior tibial, deep peroneal, common peroneal at the ankle and knee as well as the ulnar and median nerves. Studies on quantitative sensory perception in DPN have shown that there is >90% sensitivity and specificity (receiver operation characteristics) when using vibration detection threshold (VDT) and cold thermal perception (CDT). No such information is available, however, on two-point discrimination used by this cadre of surgeons. Furthermore, the variance of even CDT and VDT can be as high as 10% to 15%, making these measures unreliable as endpoints in clinical studies. Moreover, it has now been demonstrated that mechanical noise using stochastic reso-

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continued thinning and dropout of large myelinated fibers. We can surgically decompress this nerve and regain fibers, although the myelin does not recover its previous thickness.

LINK BETWEEN DIABETES AND COMPRESSION

One important implication when it comes to evaluating our patients is that over time, their symptoms are going to change. Why would diabetes predispose the nerve to chronic compression? First, the nerve is swollen. The nerve swells in a tight anatomic area, and we can postulate decreased blood flow and chronic compression. There is decreased ectoplasmic flow, and this is a slow component that means that building blocks are delayed and the nerve has to repair itself distally. We applied our chronic decompression model and showed that a diabetic banded rat was more likely to have nerve compression and be worse than the nonbanded rat.

Our hypothesis is that the symptoms are related to nerve compression. Prospective studies from what you might term a loose meta-analysis of the 14 published studies, all with the same inclusion criteria, operative technique and outcome measures, have shown good results. We have a cohort of 833 patients with this degree of magnitude of improvement and no new ulcers or amputations.

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nance can improve detection thresholds for pressure and vibration⁸ or even tactile coactivation.⁹ If only symptoms are being reported, as has occurred in the 12 reported studies, this may be no better than magnet-field therapy,¹⁰ percutaneous electrical nerve stimulation¹¹ or infrared therapy.¹² all of which have been claimed to achieve improvement in symptoms at least on a short-term basis and are noninvasive. Additionally, the results of several large 6- to 12-month clinical trials of diabetic neuropathy have been besieged by the placebo effect (Vinik Medscape) in which there have been improvements not only in symptoms but in objective measures of neuropathy presumably related to better hygiene, cessation of smoking, the use of statins and ACE inhibitors among the possible variables that affect the symptom complex of neuropathy (Tefaye ADA abstract). An extreme example of the placebo effect involved the Middlesex Hospital when 194 patients were placed on a waiting list for arthroscopy. Eighty seven (67 men) had waited >1 year with suspected meniscal tears, degenerative joint disease, ligamentous instability and sundry other complaints. At the end of a year 67% of patients who had not had surgery had recovered spontaneously!

In summary, tarsal tunnel release is being advocated as a procedure for common or garden DPN in the absence of entrapment even if there is no sign of recoverable nerve function!¹³ Unfortunately the studies reported have been of poor quality and design and it has not been possible to discern the differences in patients being treated who have only DPN from

NEW MULTICENTER TRIAL

We have trained 260 surgeons in 42 states in the United States, and 36 of these have begun entering patients into a prospective multicenter study available on the Internet at neuropathyregistry.com. So far, there are 549 patients and 40% have had their second side done. We have seen no new fractures in this group of patients.

How do we select the patient with superimposed compression? We use a positive Tinel's sign, as simple as that sign is. In this group of patients, remember before we had 69% improvement. Now, we have a positive Tinel's sign being a positive predictive value of 92%.

If we can decompress patients with active entrapment — and there are many patients with this condition — we may be able to improve their symptoms. ■

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those who have an entrapment who might indeed have benefited. The standard testing of the individuals has not been blinded and only within subjects studies are reported which are notoriously unreliable. Standard testing of distal sensory loss of small and large fiber function, eg VDT and thermal perception, strength, reflexes and nerve conduction using validated instruments would be helpful. There is a need to grade severity of entrapment, use measures of sensory tests that have been validated, the presence of a Tinel's sign, the presence of motor features and atrophy before considering surgery.¹⁴

We would recommend that before considering surgery the following caveats should be added:

- A conduction block must be present at the site proposed for decompression;
- There should not be such severe neuropathy as to preclude distinction from entrapment;
- Control sham operations should be compared with decompression for relief of symptoms if these are the only measure made; and

Objective standardized measures should be employed before and after the intervention to show bona fide improvement in nerve function.

As pointed out in a recent report from the American Academy of Neurology (*Neurology*. 2006;66:1805-1808) the utility of surgical decompression for symptomatic diabetic neuropathy would in their minds receive a Grade 1V rating, ie evidence from uncon-

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there is a discrepancy on either side, then there may be entrapment. We found that carpal tunnel syndrome was very common, and that evidence of entrapment of the tibial nerve superimposed on DPN was extremely rare.

In DPN, one sees edema of the canal with atrophy of the small muscles of the feet. What comes first? One of the major causes of DPN is microvascular insufficiency in which damage to the blood vessels by impaired function or occlusion decreases blood supply to both myelinated and unmyelinated nerve fibers. Can one recognize the patient with compression in the tunnel in the face of DPN? This may be extremely difficult.

Do we know its entrapment? Let's look at the clinical features of 1,528 hands with a neurological diagnosis of carpal tunnel syndrome; symptoms were not restricted to the hand in 31% of cases. Conclusions were wrong 40% of the time, pain was not as reliable as paraesthesiae and Tinel's sign was positive only 34% of the time. False positives in this group occurred in patients with fibromyalgia and tendonitis. In fibromyalgia there is a large proliferation of the small intraepidermal nerve fibers — the opposite of what occurs in DPN.

Is improvement due to the intervention? What about the placebo effect? Why do you see improvement in people when you operate on them, and they come out one day later and tell you everything is better? Are there ways to

cure people using nonsurgical methods such as stochastic resonance, magnetic therapy and infrared therapy? You can enhance sensation in the diabetic neuropathic foot with mechanical noise or vibration prior to testing. In these studies, however, there is no real measure of improvement, but simply a measure of changing the detection of a modality.

Dr. Dellon, however, found a 20% failure of the predictive value of a Tinel's sign. When I touch, vibrate or add pressure to one foot, the threshold in the other limb changes. So, now when I am trying to do this, if I stimulate the other limb, I will produce a reduction in the patient's ability to perceive. Now, if I stimulate the same limb, I will improve the patient's ability and if I stimulate the same limb further with noise plus measuring two-point discrimination, I will now give the patient a greatly enhanced two-point discrimination. So, this says to me, can I really trust this as a measure of what I am looking at, when I can do this with noise?

Could we possibly do damage with surgery? If you have good nerve function, you have pain. But, if you damage the system when you have pain and are through the pain threshold, pain can also disappear. We do not want to take people who have intraepidermal nerve fibers and no pain, from people who have a slight decrease and they have pain, to people who have a disappearance of pain because of complete clearance of the nerve fibers. Do not do things that potentially may hurt.

CONCLUSIONS

Decompression of multiple nerves in diabetes are being advocated by some surgeons for the treatment of common or *garden-variety* DPN. There is a need to grade the severity of entrapment, use measures of sensory tests that have been validated, the presence of a Tinel's sign, the presence of motor features and atrophy before considering surgery. A conduction block should be present, and there should not be severe neuropathy to preclude distinction from entrapment. Control and sham operations should be compared in order to determine outcomes from these procedures. Sham operations should be compared with unentrapment operations for symptoms if they are the only measure of the change, and objective standardized measures should be employed to show improvements in nerve function.

There may be a place for surgery in the treatment of common or garden-variety diabetic neuropathy. It is just that I have not been able to find it. ■

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trolled studies, case reports or expert opinion and assign the evidence a U grading which translates to unproven, the data being conflicting given the current knowledge and treatment not recommended at this point in time. Thus as I have previously concluded "there may be a place for surgical decompression of nerves in DPN but we have yet to find it." ■

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