



Practice Advisory: Utility of surgical decompression for treatment of diabetic neuropathy

Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology

Vinay Chaudhry, MD; James C. Stevens, MD; John Kincaid, MD; and Yuen T. So, MD, PhD

Abstract—Surgical decompression at the site of anatomic narrowing has been promoted as an alternative treatment for patients with symptomatic diabetic neuropathy. Systematic review of the literature revealed only Class IV studies concerning the utility of this therapeutic approach. Given the current evidence available, this treatment alternative should be considered unproven (Level U). Prospective randomized controlled trials with standard definitions and outcome measures are necessary to determine the value of this therapeutic intervention.

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Diabetic peripheral neuropathy (DPN) is a common complication of diabetes. Population-based cohort studies have shown that 66% of type I and 59% of type 2 diabetics have objective evidence of peripheral neuropathy.¹ Complications of DPN are a major cause for hospitalization among people with diabetes, and neuropathy ranks third in lifetime expenditures associated with the complications of diabetes, behind macrovascular disease and nephropathy.² Several evidence-based reviews for treatment modalities for DPN are available.^{3–7} Surgical decompression of multiple peripheral nerves is being utilized as an alternative approach to treatment of symptomatic diabetic neuropathy.^{8–15} This is based on the hypothesis that diabetic nerves are more vulnerable to compressive injury at potential sites for entrapment.^{16–18} This forms the “double crush” or “double pathology” hypothesis,¹⁹ a term originally coined for increased susceptibility of nerves with proximal and distal

compressive lesions.¹⁷ The metabolic stress of diabetes is the first crush, and compression of the nerve at the potential site of entrapment will cause the second crush. According to this hypothesis, most patients remain asymptomatic despite having diabetic nerve disease. Only when the second pathology occurs (compression of the nerves at entrapment sites) will the patients become symptomatic. Thus it has been hypothesized that symptoms in diabetic sensorimotor neuropathy may be due, in part, to compression of multiple peripheral nerves.¹⁹ Although this hypothesis has some experimental support,^{17,20–22} evidence to the contrary showing resistance to axonal degeneration after nerve compression also exists.²³

More than 240 surgeons in 41 states in the United States and in 15 different countries have been trained to perform the decompressive surgery.²⁴ As of January 31, 2006, 1,280 surgeries on 990 patients by 34 surgeons have been registered in the International Neuropathy Decompression Registry sponsored by the Diabetic Neuropathy Foundation of the Southwest (<http://www.neuropathyregistry.com/>). The public interest about this subject has generated several communications both to individuals and to organizations to develop a statement on this topic.

Additional material related to this article can be found on the *Neurology* Web site. Go to www.neurology.org and scroll down the Table of Contents for the June 27 issue to find the title link for this article.

From the Johns Hopkins Outpatient Center (V.C.), Baltimore, MD; Lutheran Medical Office (J.C.S.), Fort Wayne, IN; Indiana University (J.K.), Indianapolis; and Stanford University (Y.T.S.), Stanford, CA.

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Address correspondence and reprint requests to the American Academy of Neurology, 1080 Montreal Avenue, Saint Paul, MN 55116; e-mail: rsikka@aan.com

Due to the controversial nature of this treatment, the large number of patients with diabetes mellitus (estimated 18.2 million in the United States), and the typically progressive and irreversible nature of diabetic neuropathy, the Therapeutics and Technology Subcommittee of the AAN posed the question, "Is there evidence to support the use of decompressive surgery in the treatment of diabetic neuropathy?"

Methods. A MEDLINE, EMBASE, and PUBMED literature search was conducted by two of the authors (V.C. and J.C.S.) for all articles published between 1966 and July 2005, in the English language with the key words "diabetes mellitus," "diabetic neuropathy," and "surgical decompression." Seventy-five articles were identified by this search. An additional two articles, published in September 2005, identified after the initial search, were reviewed by two authors (V.C. and Y.T.S.). Since the intent of this review was to provide a statement for length dependent sensory motor distal neuropathy, articles solely dealing with upper extremity decompressive surgery for documented entrapments were excluded. Abstracts of the articles were reviewed and 18 full articles that pertained to the topic were selected. Accompanying editorials and related discussions were reviewed for content. The articles were classified for quality of evidence based on the AAN classification system (appendix 1). Evidence tables were constructed from 10 selected articles which dealt directly with surgical decompression in human subjects with diabetic neuropathy. This resulted in one Class III (later downgraded to Class IV) and nine Class IV studies being identified for the purpose of this Practice Advisory.

Results. Eleven articles were identified that dealt with decompressive surgery for the treatment of diabetic neuropathy (table E-1 on the *Neurology* Web site at www.neurology.org). There was only one prospective study that employed blinded outcome assessment in a small cohort of patients.¹⁰ This article was downgraded to Class IV because of a lack of detail concerning nerve conduction studies, lack of definition and lack of clarity in segregating patients into peripheral neuropathy or compression categories, and use of arbitrarily defined scales of improvement. However, this study was prospective, with a blinded evaluator, and involved a consecutive series of eligible patients with "symptomatic" diabetic neuropathy determined by subjective report and the presence of a Tinel's sign over an involved peripheral nerve entrapment site. This series consisted of 20 patients (14 type I and 6 type II diabetics) who underwent a total of 31 nerve decompression procedures. Electrodiagnostic studies were performed preoperatively in each patient and showed that 22% had nerve compression, 56% had a peripheral neuropathy with superimposed nerve compression, and 22% had a peripheral neuropathy without a superimposed nerve compression (the details of how these diagnoses were reached was not provided). Patients were assessed preoperatively and postoperatively with a standardized two-point discrimination test using the Pressure-Specified Sensory Device (Sensory Management Services, LLC).²⁵ The postoperative examination was administered to 14 patients (six patients elected to have bilateral extremity decompression procedures) by a blinded therapist. Surgical scars were covered by clothing and the operated limb was compared to the contralateral nonoperated side. Improvement was considered to have occurred if the two-point discrimination changed from "absent" to "any numerical value" or demonstrated a decrease of >2 mm. Postoperative assessment was performed at a mean of 23.3 months (range 12 to 41 months) after the procedure.

This study revealed that 79% of the surgically decom-

pressed nerves improved in their two-point discrimination test postoperatively. None of the decompressed nerves worsened, whereas 32% of the contralateral non-treated nerves worsened in their two-point discrimination ($p < 0.001$). Twenty-one percent of the surgically treated nerves and 59% of the non-surgically treated nerves remained unchanged at follow-up assessment. The author did not report the results according to the preoperative electrodiagnostic studies. Therefore, one cannot discern whether the positive results were due to decompression of "compressed" nerves as determined by electrodiagnostic studies or decompression of diabetic peripheral neuropathy without a superimposed nerve compression.

The remaining 10 studies^{8,9,11-15,26-28} were comprised of non-blinded case series reporting results of decompression of the posterior tibial, deep peroneal, common peroneal at the ankle and knee, median and ulnar nerves at the wrist and elbow, with one study⁸ that also included decompression of the radial nerve in the forearm. The assessments used a variety of outcome measures, all collected by the operating surgeon. Eight of the 10 studies reported a reduction in subjectively reported pain (80 to 92% of the treated patients), as well as an improvement in two-point discrimination (67 to 79% of the treated patients). The number of patients in these series who had "diabetic neuropathy" ranged from a minimum of 10 to a maximum of 60. Definitions for what constituted diabetic neuropathy and the methodology for pain measurement/reporting were non-uniform between the studies. One study¹⁴ involved a questionnaire/phone interview of 50 patients who had previously undergone unilateral lower extremity nerve decompression surgery to determine if the non-operated limb had a propensity to develop ulcerations or require amputation at a greater rate than the surgically treated extremity. The surgeon reported that none of the surgically treated limbs developed ulcers or required amputation whereas 12 patients developed ulcers and three required amputations in their non-surgically treated leg or foot ($p < 0.001$). The mean follow-up period was 4.5 years (range 2 to 7 years). There was no indication that the limbs were examined by the independent investigators.

Discussion. The current evidence supporting the utility of decompressive surgery for the treatment of diabetic neuropathy is of poor quality and design. Although purported as a potential alternate therapy for this progressive and often debilitating condition, the data are insufficient to support or refute its benefits. None of these studies provided randomization or a control group (other than one weak Class III study which was downgraded to Class IV, in which the patient served as his or her own control). The patients and evaluators were unblinded in 9 of the 10 studies, allowing the opportunity for significant bias in determining outcomes. The definition of peripheral neuropathy in these studies is unclear.

The standard testing of distal sensory loss of small and large fiber modalities (outside of two-point discrimination), distal weakness, deep tendon reflexes, gait, and Romberg's testing were not included in these studies. Only a few⁸⁻¹⁰ report the performance of nerve conduction studies, but specific data were not provided. One cannot discern whether the positive results re-

ported were simply due to release of traditionally compressed nerves as would be determined by electrodiagnostic studies, or the result of treatment of a process that would be considered a symmetric diabetic sensorimotor neuropathy. In a majority of the studies, improvement was based on subjective measures and observations of the operating surgeon. Precise description of the location and degree of improvement was not clear in many of these reports. The statistical analyses utilized have nonstandardized measurements.

Conclusions and recommendations. There are inadequate data concerning the efficacy of decompressive surgery for the treatment of diabetic neuropathy. Given our current knowledge, this treatment is unproven (Level U) (see appendix 2 for classification of recommendations).

Recommendations for future research.

1. Randomized controlled trials with standard definitions of peripheral neuropathy, control for concurrent treatments, and validated functional outcome measures with independent, blinded evaluations should be performed.
2. Distinction between entrapment neuropathy and peripheral sensorimotor neuropathy should be clarified in these studies.
3. Monitoring of glycemic control should be conducted and well-documented in future studies.
4. Detailed reporting of postoperative complications should be included in all future studies.
5. Data should be provided to allow calculation of number needed to treat to result in a benefit (NNT) and the number of surgeries required to result in harm to the patient (NNH).

Disclaimer. This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

Mission statement. The Therapeutic and Technology Assessment Subcommittee (TTA) oversees the development of AAN technology assessments and therapeutic assessments, which are evidence-based statements that assess the safety, utility and effectiveness of new, emerging, or established therapeutic agents or technologies in the field of neurology. Technology assessments and therapeutic assessments are developed through a rigorous process of defining the topic, evaluating and rating the quality of the evidence, and translating the conclusions of the evi-

dence into practical assessments that can be used to guide the use of technologies and therapeutic agents in the practice of neurology.

Appendix 1

Classification of evidence for therapeutic articles

Class I: Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required:

- a) Primary outcome(s) is/are clearly defined.
- b) Exclusion/inclusion criteria are clearly defined.
- c) Adequate accounting for drop-outs and cross-overs with numbers sufficiently low to have minimal potential for bias.
- d) Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class II: Prospective, matched, group cohort study in a representative population with masked outcome assessment that meets a-d above OR a RCT in a representative population that lacks one criterion a-d.

Class III: All other controlled trials including well-defined natural history controls or patients serving as own controls in a representative population, where outcome assessment is independently assessed or independently derived by objective outcome measurement (an outcome measure that is unlikely to be affected by an observer's [patient, treating physician, investigator] expectation or bias [e.g., blood tests, administrative outcome data]).

Class IV: Evidence from uncontrolled studies, case series, case reports, or expert opinion.

Appendix 2

Classification of recommendations

- A = Established as effective, ineffective, or harmful for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)
- B = Probably effective, ineffective, or harmful for the given condition in the specified population. (Level B rating requires at least one Class I study or at least two consistent Class II studies.)
- C = Possibly effective, ineffective, or harmful for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)
- U = Data inadequate or conflicting given current knowledge, treatment is unproven.

Appendix 3

Therapeutics and Technology Assessment Subcommittee Members: Janis Miyasaki, MD (co-chair); Yuen T. So, MD, PhD (co-chair); Carmel Armon, MD, MHS (ex-officio); Vinay Chaudhry, MD; Richard M. Dubinsky, MD, MPH; Douglas S. Goodin, MD (ex-officio); Mark Hallett, MD; Cynthia Harden, MD; Kenneth J. Mack, MD, PhD; Fenwick T. Nichols III, MD; Michael A. Sloan, MD, MS; James C. Stevens, MD.

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