

# Prevention of Ulceration, Amputation, and Reduction of Hospitalization: Outcomes of a Prospective Multicenter Trial of Tibial Neurolysis in Patients with Diabetic Neuropathy

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## Abstract

This is the first multicenter prospective study of outcomes of tibial neurolysis in diabetics with neuropathy and chronic compression of the tibial nerve in the tarsal tunnels. A total of 38 surgeons enrolled 628 patients using the same technique for diagnosis of compression, neurolysis of four medial ankle tunnels, and objective outcomes: ulceration, amputation, and hospitalization for foot infection. Contralateral limb tibial neurolysis occurred in 211 patients for a total of 839 operated limbs. Kaplan–Meier proportional hazards were used for analysis. New ulcerations occurred in 2 (0.2%) of 782 patients with no previous ulceration history, recurrent ulcerations in 2 (3.8%) of 57 patients with a previous ulcer history, and amputations in 1 (0.2%) of 839 at risk limbs. Admission to the hospital for foot infections was 0.6%. In patients with diabetic neuropathy and chronic tibial nerve compression, neurolysis can result in prevention of ulceration and amputation, and decrease in hospitalization for foot infection.

## Keywords

- ▶ ulcers
- ▶ amputation
- ▶ diabetic neuropathy

Over the 18 years since the first publication of a retrospective, Level IV study of the results of decompression of multiple sites of peripheral nerve compression in the upper and lower extremity,<sup>1</sup> subsequent similar studies confirmed that 80% of patients can expect good relief of their pain, that 80% of the patients can expect recovery of some sensation, and that new ulcers and new amputations can be largely prevented.<sup>2–15</sup> These studies have been reviewed recently, and have in common the identification of the site of chronic nerve entrapment using the Tinel sign, surgical release of the tibial nerve in the four medial ankle tunnels, and early ambulation.<sup>16,17</sup> Three separate basic science laboratories have documented in animal models of diabetes that the peripheral

nerve is susceptible to compression and that decompression will improve peripheral nerve function in the presence of a diabetic neuropathy.<sup>17–22</sup> The controversies related to this approach have also been reviewed recently.<sup>23</sup>

It is the purpose of this report to describe the results of the first prospective, multicenter nonrandomized trial of neurolysis of the tibial nerve and its branches in the tarsal tunnel, with the data collection being done prospectively and analyzed prospectively with Kaplan–Meier proportional hazard analysis. The study was done sufficiently long and with a sufficiently large well-defined patient population to demonstrate the outcome of this approach upon ulcer and amputation occurrence, and hospitalization for foot infections.

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## Methods

This study was designed as a prospective, multicentered study, with a well-defined sample of patients and well-defined outcomes.

Each of the 38 surgeons participating in this study, were trained in an Advanced Lower Extremity Peripheral Nerve Surgery Workshop so that each surgeon used the same operative technique as previously described and reviewed,<sup>23</sup> and each used the same outcome measurements.

### Inclusion Criteria

1. Patient had to have diabetes requiring medication for glycemic control.
2. The patient's diabetes was in good glycemic control.
3. Patient had to have symptomatic diabetic neuropathy, defined as a diffuse, symmetrical, distal, large fiber, and polyneuropathy.<sup>24–26</sup>
4. This neuropathy had to be documented at least by neurosensory testing with the pressure-specified sensory device.<sup>27–30</sup>
5. If the patient had pain, then there had to be a trial and failure of neuropathic pain medication.<sup>31,32</sup>
6. Patients had sufficient lower extremity blood supply, as demonstrated either by a palpable dorsalis pedis or posterior tibialis pulse, or, in the absence of a palpable pulse, an ankle/brachial index  $>0.70$ .
7. Absence of pedal edema.
8. Physical findings consistent with a chronic nerve compression at the known sites of anatomic narrowing, that is, common peroneal nerve at the fibular tunnel, deep peroneal nerve over the dorsum of the foot, and tibial nerve compression in the tarsal tunnel, as demonstrated by a positive Tinel sign.<sup>8</sup>
9. Patient had to be sufficiently healthy to have a 2-hour general anesthetic.

### Exclusion Criteria

1. Weight over 300 pounds.
2. Previous lower extremity peripheral nerve surgery.
3. Previous amputation.
4. Presence or absence of ulcerations was not an exclusion criteria but was noted for substratification data analysis.

### Outcome Analysis

1. Presence or absence of ulceration anywhere on the operated foot.
  2. Any lower extremity amputation in the postoperative period on the operated foot.
  3. Hospitalization for infection in the operated foot.
- Statistical analysis was done using Kaplan–Meier proportional hazard analysis and student's *t*-test.

## Results

At the time of data analysis, 628 patients had been enrolled in the study and followed for at least 1 year. Of these, 211 had the

contralateral limb operated upon for a total number of operated limbs of 839. Of the 628 patients, 465 (74%) had pain  $>5$  at the initial visit, and 152 of these patients had a second limb operated upon for a total of 617 operated limbs with pain. Data analysis extends from the initial onset to 3.5 years postoperatively.

The results for appearance of a new ulceration are given in ►Fig. 1. Of the 782 limbs that were operated and had never had a previous ulceration, just 2 patients (0.3%) developed an ulceration at 1.5 years and this percentage did not increase in the remaining period of observation.

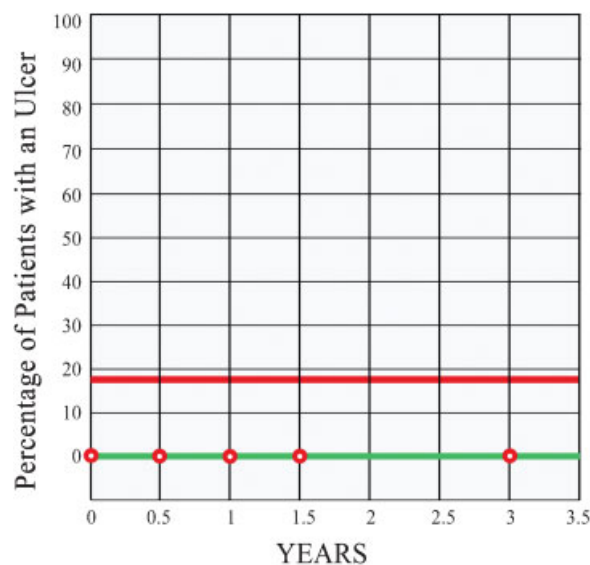
The results for recurrent ulceration in those patients who had a pre-existing ulcer or healed ulcer are given in ►Fig. 2. Of the 57 limbs that had a previous history of ulceration, just 2 had a recurrent ulceration (3.8%) over the period of observation.

The results for occurrence of any amputation are given in ►Fig. 3. Of the 839 limbs that were operated upon, a toe amputation occurred in 1 patient (0.2%).

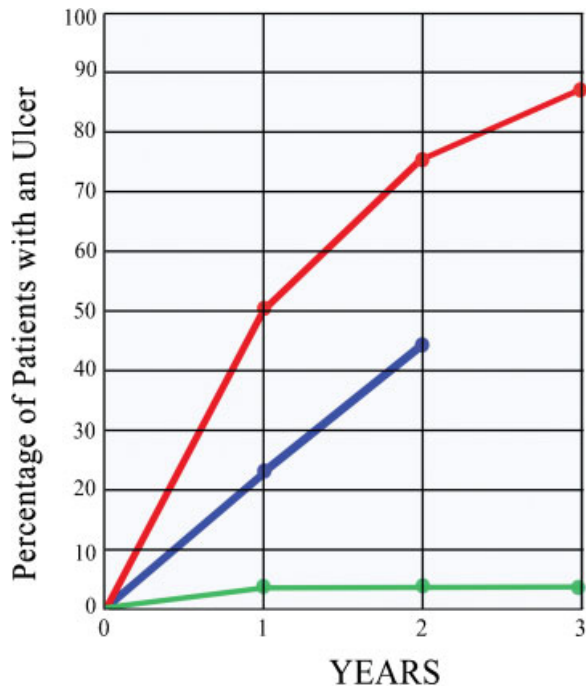
The results for hospitalization for foot infection are given in ►Fig. 4. Of the 628 patients, 4 (0.6%) were admitted to the hospital for treatment of a foot infection that was not related to the surgical healing process over the period of observation.

## Discussion

The results of this study demonstrate that patients with symptomatic neuropathy related to diabetes can have unrecognized lower extremity chronic nerve compression in the four medial ankle tunnels, and, when this is present, neurolysis of the tibial nerve predictably will prevent new ulceration and amputation, and reduce hospitalization from foot infections. The patients in this study remained diabetic,



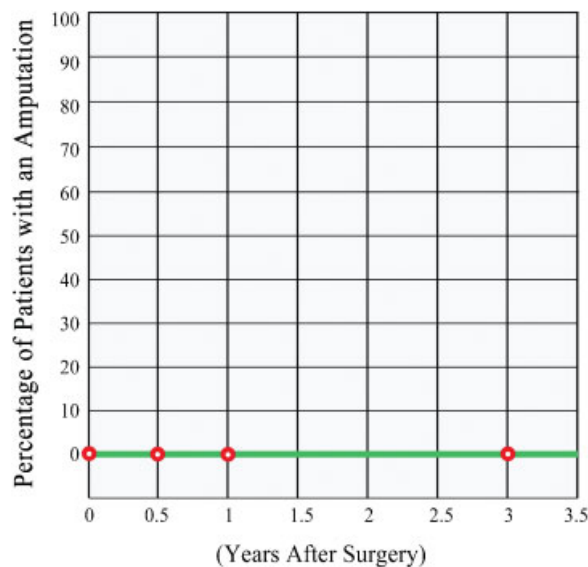
**Figure 1** Outcome: New ulceration. Of the 782 limbs that were operated upon that had never had a previous ulceration, just two patients (0.3%) developed an ulceration at 1.5 years and this percentage did not increase in the remaining period of observation (green line). The expected lifetime occurrence of ulceration in this population of patients is 15% (red line).



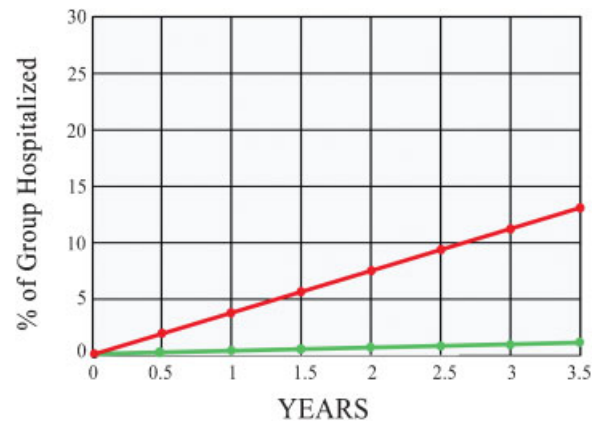
**Figure 2** Outcome: Recurrent ulceration. Of the 57 limbs that were operated upon that had a previous ulceration, 2 (3.8%) recurred (green line). It is expected that from 50 to 60% of healed ulcers will recur (red line), and with intensive primary foot care the recurrence rate can be reduced to 25 to 30% (blue line).

they just no longer had compression of their tibial nerve at the ankle level, and this permitted recovery of sensation with all its protective benefits.

Prevention of ulceration and amputation in patients with diabetes remains the elusive quest. About 20 years ago, reviews of the medical literature documented that the incidence of ulceration is 2.5% per year and its prevalence is 15%.<sup>33-36</sup> Despite attempts to decrease the number of



**Figure 3** Outcome: Amputation. Of the 839 limbs that were operated upon, an amputation occurred in one patient (0.2%). The expected number of amputations would be 10 to 15%.



**Figure 4** Outcome: Hospitalization for foot infection. Of the 628 patients that were operated upon, 4 (0.6%) were admitted to the hospital for treatment of a foot infection that was not related to the surgical healing process (green line). This may be compared with the published results from another study of the best available, intensive primary foot care, in which, of 1666 patients followed for 2 years, 9% developed a foot infection, and 3.7% of patients required hospitalization (red line).<sup>49</sup>

amputations in the United States of America by various strategies from better glucose control, to monitoring screening exams for impaired sensibility, the number of amputations continued to increase from 54,000 in 1990,<sup>37</sup> to 92,000 in 1999.<sup>38</sup> More recently, from 2000 to 2002, an estimated 11.7% of U.S. adults with diabetes still had a history of foot ulcer.<sup>39</sup> This has been the basis for the teaching that the natural history of diabetic neuropathy is progressive and irreversible. However in 2004, based upon the hypothesis that some of the symptoms of diabetic neuropathy were due to superimposed nerve compressions, the impact of tibial neurolysis at the ankle on the development of ulcers and amputations in both the operated and the contralateral, non-operated limb was evaluated in a retrospective analysis of 50 diabetics a mean of 4.5 years (range 2 to 7 years) from the date of surgery. No ulcers or amputations occurred in the index limb of these patients. In contrast, there were 12 ulcers and 3 amputations in 15 different patients in the contralateral limbs. This difference was significant at the  $p < 0.001$  level. It was concluded that decompression of lower extremity nerves in diabetics with chronic nerve compression changes the natural history of this disease, representing a paradigm shift in health care costs.

Review of the world literature today with respect to what has happened during the past twenty years with regard to implementation of medical programs to prevent ulcers and amputation remains discouraging. The incidence of foot ulcerations is 1.9 to 4.1% per year, with a prevalence of 4 to 18% of the diabetic population.<sup>40-42</sup> The lifetime risk for developing an ulcer may still be as high as 25%<sup>40</sup> The situation for amputations is quite similar. In diabetic patients, the incidence of both major and minor lower-extremity amputations ranges from 2.1 to 13.7 per 1000.<sup>43</sup> While certain well controlled populations, such as in Norway, have demonstrated improvement in the incidence of diabetic major lower extremity amputations from 4.0 to 2.4 per 1000 diabetics per

year through an intense program of patient education and examination,<sup>44</sup> most reports are still discouraging. In the United Kingdom, in 2008, the absolute number of diabetes-related amputations increased by 14.7%.<sup>45</sup> In that study, while the incidence of amputations decreased by 9.1%, the absolute magnitude of the amputations was still at 2.5 per 1000 people with diabetes, and the incidence of minor and major amputations did not significantly change. In Saudi Arabia, in 2010, comparison of two small (20-patient) cohorts of patients, with and without instruction in foot care, saw the amputation rate remain at 69%.<sup>46</sup> In the United States, in 2010, a study was reported that demonstrated that while the number of limb losses decreased, the frequency of total amputations increased from 24 in the first year of the study to 46 in the second year of the study.<sup>47</sup>

These disturbing statistics highlight the need to consider evaluating diabetics with neuropathy for the presence of chronic nerve compression of the tibial nerve in the tarsal tunnels. This failure to achieve significant change by medical management should be contrasted with the results of the present surgical study which show an incidence of new ulcerations of just 0.6% and recurrent ulcerations of just 3.8%. A recent surgical review<sup>48</sup> of recurrent ulcerations in a cohort of 75 feet in 57 patients that had a neurolysis of the tibial nerve in the four medial ankle tunnels, the same technique as reported in the present study, found a recurrence rate of 4.9% with a mean follow-up of 2.9 years (range 1–13 years), again demonstrating the significant improvement that can be achieved if a proactive approach to restoring sensation is adopted for the management of this problem.

This is the first study to report the effect of neurolysis of the tibial nerve in the tarsal tunnel on the outcome of hospitalizations for foot infections. As a comparison, consider the intensive program of preventive foot care described by Lavery et al in 2006.<sup>49</sup> Among 1666 diabetics with neuropathy, who were receiving regular podiatric foot care and preventive techniques, 9% developed foot infections and 3.7% required hospitalization for treatment of foot infections over their 2-year time period of observation. This may be contrasted to the results of the present study (→ Fig. 4) in which just 0.6% of patients who had neurolysis of the tibial nerve required hospitalization for treatment of foot infections over the 2-year time period of observation.

#### Note

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#### Conflict of Interest

A. Lee Dellon, M.D., Ph.D., owns Sensory Management Services, LLC, which markets the Pressure-Specified Sensory Device™.

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