Journal of Diabetes and Metabolism
Garrod et al., J Diabetes Metab 2014, 5:1
DOI: 10.4172/2155-6156.1000330
Research Article Open Access

Prevention of Ulceration and Amputation, by Neurolysis of Peripheral Nerves in Diabetics with Neuropathy and Nerve Compression: Decision-tree Utility Analysis

Krista Garrod[1], Scott LaJoie A[1], Steve McCabe[2]* and Lee Dellon A[3]

[1]*University of Louisville, USA*
[2]*University of Toronto, USA*
[3]*Plastic Surgery & Neurosurgery, Johns Hopkins University, USA*

Abstract

The historical consequences of diabetic neuropathy are loss of sensibility with its consequences; foot ulceration and amputation. The purpose of this decision-tree analysis is to evaluate the effectiveness of medical management versus surgical decompression in patients presenting with diabetic neuropathy and superimposed chronic tibial and peroneal nerve compressions. A decision-tree analytic approach was utilized to achieve a reasonable efficacy estimate. The study is limited by the uncertainty associated with utility values, probabilities, and complication rates. Other limitations to this model include lack of randomized controlled trial data, and assumed patient compliance with either the medical or surgical treatment strategies. Based upon the available evidence from the literature, this model demonstrates the potential advantage of the strategy of decompression surgery for treatment of diabetic neuropathy with superimposed tibial and peroneal nerve compressions.

Keywords: Decision tree analysis; Diabetic neuropathy; Neurolysis

Introduction

Diabetes mellitus, a chronic metabolic disorder, is currently considered an epidemic, with an estimated 26million Americans and 285million people globally affected as of 2010. The incidence of diabetes is expected to nearly double by 2030. Further, the Centers for Disease Control and Prevention (CDC) projects that current trends forecast as many as 1 in 3Americanadults could have diabetes by 2050 [1,2]. As the incidence and prevalence of diabetes is growing exponentially, related complications are also rising. Specifically, peripheral neuropathy is one of the most common, costly, and disabling complications of diabetes. Development of neuropathy occurs most often in the feet, and includes clinical morbidities of pain, motor dysfunction, and loss of sensation, ulcers, infections, gangrene, and amputation. Historically considered progressive and irreversible, peripheral neuropathy and sensory loss is considered the leading risk factor in the development of ulcers [3-5]. The magnitude of diabetic complications is staggering, especially progressive diabetic foot neuropathy. Thus, new treatment modalities are needed.

Historically, surgical treatment for diabetic neuropathy was reserved for wound care or amputation. However, there is an alternative surgical procedure for alleviation of diabetic foot pain and loss of sensation. The surgical technique has been well-described, and in brief requires decompression of the four medial ankle tunnels, typically termed the "tarsal tunnel", a neurolysis of the common peroneal nerve at the fibular head, and a neurolysis of the deep peroneal nerve over the dorsum of the foot [6]. It has been suggested decompression of chronic tibial and peroneal nerve compressions, superimposed upon the underlying neuropathy, could restore some sensation and there by minimize occurrence of ulcers and amputations [7-13].

This approach stems from research demonstrating that diabetic neuropathy symptoms are similar to that of chronic nerve compression. Further research demonstrated physiological evidence that peripheral nerves are susceptible to compression in patients with diabetes [12,14,15]. The prevalence of patients presenting with diabetic neuropathy and superimposed chronic tibial and peroneal nerve compressions is estimated between 33% and 50% [16-18]. The delineation of the patient for whom this nerve decompression is appropriate is: a) someone with diabetes, b) who has symptoms of numbness and or pain in both feet, who is c) under good glycemic control, and who d) has not been helped with neuropathic pain medication, who has, on physical examination e) a positive Tinel sign over the tibial nerve in the tarsal tunnel. This is further depicted in the potential treatment algorithm (Figure 1).

Under the premise of this approach, significant reduction in symptoms, complications, and targeted outcomes, such as ulceration and amputation, are reported. Literature review of nerve decompression surgery in this population of patients reveals marked improvements in pain reduction, sensation recovery, and prevention of ulcers and amputations. Overall, results indicate that 80% of patients have good relief of pain and that 80% of patients have some sensation recovery. Most studies reported that ulcers and amputations are largely prevented [18]. Recent data of a large multicenter prospective study reported a reduction of ulcer recurrence to 0.3%, and 0.2% amputation occurrence post decompression surgery [19].

Though surgical intervention is an expensive therapeutic modality, the potential beneficial outcomes cannot be discounted. It is the

***Corresponding author:** Steve McCabe, Toronto Western Hospital, 399 Bathurst Street, Toronto, ON M5T 2S8, USA, Tel: (416) 603-5455; Fax: (416) 603-5392; E-mail: Steve.Mccabe@uhn.ca

Received December 26, 2013; **Accepted** January 25, 2014; **Published** January 29, 2014

Citation: Garrod K, Scott LaJoie A, McCabe S, Lee Dellon A (2014) Prevention of Ulceration and Amputation, by Neurolysis of Peripheral Nerves in Diabetics with Neuropathy and Nerve Compression: Decision-tree Utility Analysis. J Diabetes Metab 5: 330. doi:10.4172/2155-6156.1000330

Citation: Garrod K, Scott LaJoie A, McCabe S, Lee Dellon A (2014) Prevention of Ulceration and Amputation, by Neurolysis of Peripheral Nerves in Diabetics with Neuropathy and Nerve Compression: Decision-tree Utility Analysis. J Diabetes Metab 5: 330. doi:10.4172/2155-6156.1000330

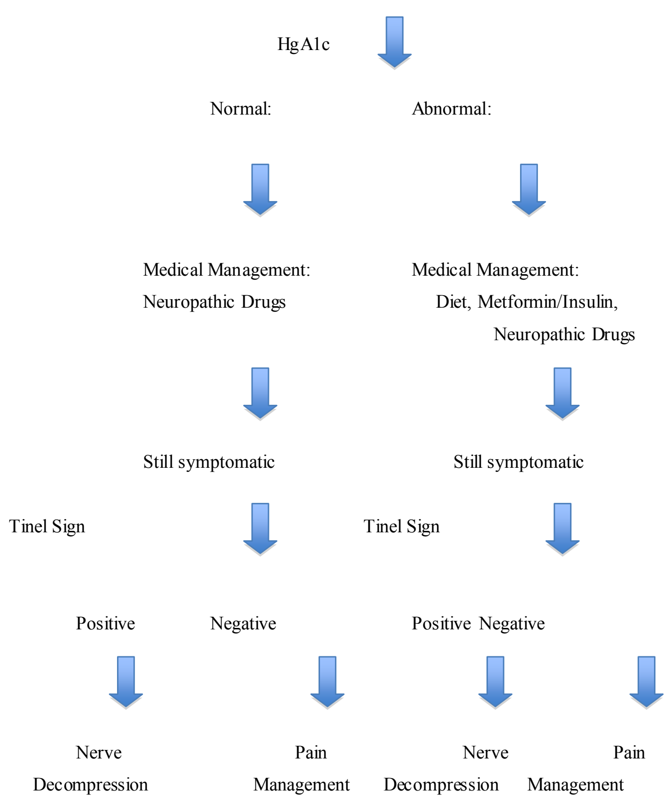

Figure 1: Diabetic with Symptoms of Numbness/Tingling/Pain in Feet.

purpose of this decision analysis to further analyze two strategies for comparison of the treatment of diabetic neuropathy in the lower extremity: medical management and decompression surgery.

Materials and Methods

Decision analysis

Decision analysis was performed using statistical software (TreeAge 2012 software package; TreeAge Software, Williamstown, MA). Decision analysis has been shown to be an accurate and reliable methodology that promotes optimization of decision making based on best available evidence. The process of this analysis involves creating a decision tree to structure the issue, the development of utilities and outcome probabilities, rollback analysis to ascertain the optimal approach, and sensitivity analysis to demonstrate the effect of varying utilities and outcome probabilities on decision making. A utility is a subjective measure of the strength of preference an individual has for an outcome; in recent years, as medicine places more importance on shared decision making, the patient's utility can be seen as representing the value the patient places on possible treatment outcomes. Decision tree analysis is an effective tool to assess comparative medical interventions when data are lacking or conflicting in the evaluation of efficacy and clinical outcomes. This tree analysis utilizes data available in the medical literature to produce a model of outcome probabilities and possible utilities associated with a particular management strategy.

Outcomes of interest

This model focuses on the complication endpoints of ulcer and amputation.

Outcome probability estimates: For this study, outcome probabilities were determined by are view of the literature. PubMed and Google Scholar internet searches using combinations of keywords "diabetic neuropathy, nerve compression, surgical management, decompression surgery" as well as population diabetic probabilities for medical management estimations, and diabetic neuropathy for outcomes of ulcer and amputation. Further data were obtained by manually reviewing each of the references cited in articles retrieved. The surgical decompression literature was recently summarized in a review by Dellon [18]. Therefore, the 2008 summary article and a post-2008 review of the aggregated literature identified two additional articles of relevant patient data [19,20] to be utilized for the statistical model.

Although the likelihood of developing recurrent ulcers is higher than initial ulcer development, in order to obtain a conservative estimation, new and recurrent ulcer figures were not stratified in the decompression surgery population for this analysis. Specific probabilities utilized in this decision tree model are summarized in Table 1. Of note, surgical complications were not fully described in the available literature; therefore probabilities for outcomes did not differ between post-operative complications and those without surgical complications for this analysis. The ranges for probabilities were also obtained from the literature.

Outcome utility estimates

Outcome utility values represented patient preferences for various disease states. Utility values range from0to1, understood as the worst

	Baseline	Range
Probabilities		
Diabetic Neuropathy No Ulcers p_DN	0.7	0.55-0.85
Diabetic Neuropathy Ulceration p_DNUlc	0.3	0.15-0.4
Diabetic Neuropathy Re-Ulceration p_DNreUlc		0.5-0.6
Diabetic Neuropathy Amputation p_DNAmp	0.05	0.02-0.15
Diabetic Neuropathy , Surgery, PostOp Complications p_SxComp	0.15	0.10-0.20
Diabetic Neuropathy , Surgery, No PostOp Complications p_DNSx	0.85	0.8-0.9
Diabetic Neuropathy , Surgery, Ulcer p_DNSxUlc	0.02	0-0.04
Diabetic Neuropathy , Surgery, Amputation p_ DNSxAmp	0.015	0-0.03
Utilities*		
Diabetic Neuropathy , Ulcer free U_DN	0.84	0.81-0.87
Diabetic Neuropathy , Ulcer U_DNUlc	0.75	0.71-0.79
Diabetic Neuropathy , Amputation U_DNAmp	0.68	0.63-0.72
Diabetic Neuropathy, Surgery, No PostOp Complications, Ulcer free U_DNSx	0.89	0.79-0.99
Diabetic Neuropathy, Surgery, No PostOp Complications, Ulcer U_DNSxUlc	0.79	0.69-0.89
Diabetic Neuropathy, Surgery, No PostOp Complications, Amputation U_DNSxAmp	0.71	0.61-0.81
Diabetic Neuropathy, Surgery, PostOp Complications, Ulcer free U_DNSxComp	0.81	0.71-0.91
Diabetic Neuropathy, Surgery, PostOp Complications, Ulcer U_DNSxCompUlc	0.72	0.62-0.82
Diabetic Neuropathy, Surgery, PostOp Complications, Amputation U_DNSxCompAmp	0.65	0.55-0.75
DisUtility, reduction for surgical procedure	.03	
Utility, increase for post surgery (non-complication) symptom improvement	10%	

*Baseline and range utility values are calculate estimations adapted from literature

Table 1: Variables used in decision analysis- Baseline values and ranges.

cases cenario or death ranging incrementally to a perfect-disease free health state. There are several methods for obtaining utility values related to clinical outcomes including visual analog scale, time trade-off calculations, standard gamble, quality of life questionnaires, and population or expert opinion rankings.

For this model, utilities were obtained from the literature of health states involving foot ulcers and amputations. Redekop et al. specifically addresses the disease under study and targeted outcomes. Due to the parallel evaluations, this data was utilized for this analysis. Redekop utilities were determined by time trade-off interviews in the general population, the mean utility values were then adjusted for the outcomes based on the utility value of a having diabetes [21]. The values for decompression surgery were further adjusted to compensate for the additional variables.

Because surgery itself carries an inherent risk, a disutility for undergoing surgical procedure was estimated. In order to adjust for decompression surgery, utilities for ulcer and amputation were decreased by the difference in the reported values for surgical intervention equal to half of the value difference reported for toe amputation to foot amputation by Redekop et al. [21].

< (Utility toe Amp- Utility_foot amputation)*I* 2>

This again is a conservative calculation as decompression surgery is at ransient health state and may not have as much value as a toe amputation procedure which would be a permanent surgical change in health state.

Though discounted for surgical procedure, the final utility for not developing an ulcer after surgery was calculated with a small increased value based on the assumption that this represents an increased health state (decrease in symptoms); whereas without surgical intervention it is assumed that the health state continues and simply does not worsen. This implicitly assumed the state of reduced problem-specific symptoms of diabetic neuropathy and not to the absence of diabetes. No literature addresses utility or quality of life assessments following this particular surgery, however the literature does support a minimum improvement of pain of 75% [22]. Therefore, a modified decomposed strategy was employed to calculate utility values.

<Utility_Diabetic Neuropathy + Utility_Post Surgical Symptom Improvement (10%)- DisUtility_Surgical procedure>

To illustrate, calculation of no ulcers developing after complication free decompression surgery is as follows: Utility of medical management and not developing ulcers=0.84

0.84* 0.10=0.0840.84+ 0.08-0.03=0.89

However, this improvement was not added to those utilities with surgical complications following decompression surgery so as not to over value symptom reduction when experiencing post-operative complications.

Decision tree and rollback analysis

A simple decision tree was constructed with 1 decision node, 7 chance nodes, and 9 terminal nodes (Figure 2). The decision tree model demonstrates two differing management strategies for diabetic neuropathy. The decision node divides into two branches: medical management and surgical decompression. Both branches are followed by chance nodes, each one ultimately terminating in a clinical outcome. Per convention, probability data were placed under the terminal nodes and utility values to the right of the terminal nodes.

Rollback analysis mathematically incorporates outcome values by multiplying and adding across nodes with in a particular branch. This results in a calculated 'expected utility' for each outcome by the model thus illustrating the management strategy associated with the highest calculated value being optimal for the given utilities and probabilities. Rollback was performed on this model to identify the optimal management strategy (Figure 3).

Sensitivity analysis

One-way sensitivity analyses were performed to model the impact on decision making of varying utility and probability values. The utility and probability ranges are represented in Table 1. The probabilities for both modalities and medical management utility values were obtained from the literature; the utility values for decompression surgery variables are calculated estimates. Utilities adapted from Redekop were given ± 0.10 calculated ranges in order to determine the strength of the estimations. One-way sensitivity analyses were performed on all variables in the model. This provided a better illustration of the variables, their interaction, and influence on the model.

Results

For nonsurgical treatment and surgical decompression, the obtained probabilities and utilities are available in Table 1. The systematic review

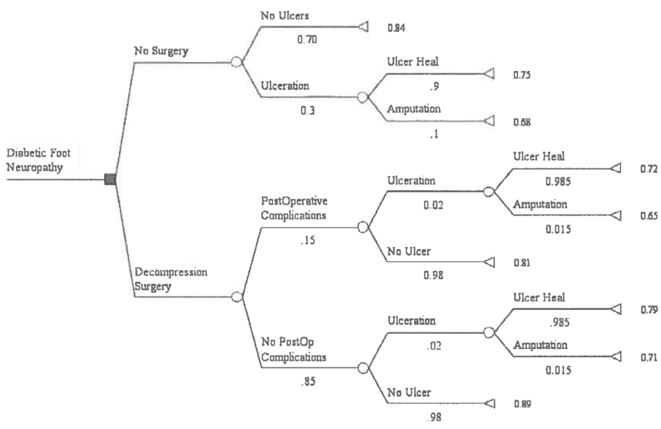

Figure 2: Decision tree for medical management versus surgical decompression. Decision nodes are represented by a square, chance nodes are represented by a circle, and terminal nodes are represented by a triangle. Probabilities and utilities are estimated from the published literature.

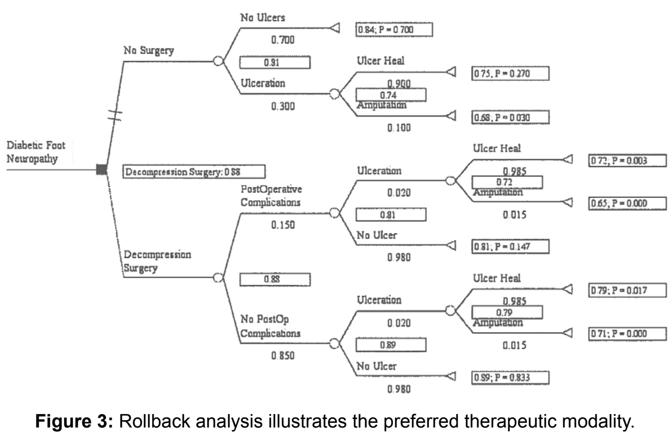

Figure 3: Rollback analysis illustrates the preferred therapeutic modality.

and calculated estimation of values appear to make sense or pass "face validity" when assessed in rank order of utility values. Rollback analysis identified the expected value of surgery as 0.88 (Figure 3). For the surgical strategy option, the significance of preventing ulceration was p<.002 and for preventing amputation was p<.001. The results of the decision tree model mirror the observed results in published literature. The model follows the clinical experience and illustrates that surgical decompression is the favored decision alternative.

Varying the probability or utility values may change the decision-making process within the estimated ranges. For this analysis, one-way sensitivity analyses were performed on all variables in the model over proposed ranges. The model appears robust, as it is only sensitive to change within a proposed range for one variable: utility of decompression surgery with no post-surgical complications or outcomes are reported. As represented in Figure 4, if the success of decompression surgery with no surgical complications, and no development of ulcers is valued below 0.812, medical management is the preferred therapy.

Discussion

Diabetic neuropathy in the lower extremity, even with good attempts at euglycemia and foot care, all too often still lead to ulceration and/or amputation [23]. While no medical treatments are known to be effective treatment of progressive pain and sensory loss associated with diabetic neuropathy, proponents of medical management proclaim a number of randomized controlled clinical trials which have shown that meticulous control of blood glucose dramatically reduces the frequency and progression of diabetic complications [23]. In contrast, the hypothesis that diabetic neuropathy creates susceptibility for chronic nerve compression, and that decompression of chronic compression of the tibial and peroneal nerves in the diabetic with neuropathy can restore sensation, preventing the risk of ulceration and amputation [24], offers a clear management alternative choice. The present decision tree analysis demonstrated that the surgical choice, given the assumptions of the model, offers a cost-effective strategy to society to reduce ulceration, p<.002, and reduce amputation, p<.001.

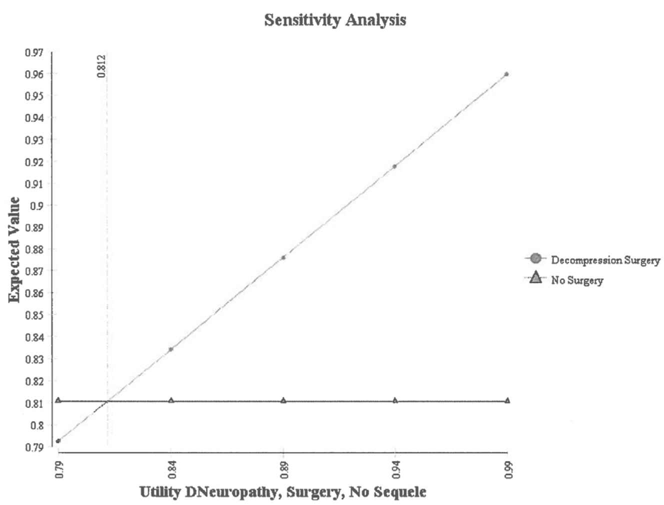

Figure 4: Sensitivity analysis of the estimated utility of decompression surgery. Lines represent the expected value (EV) for the decision to manage with medical therapy or decompression surgery. The strength of the preferred modality is represented by a threshold value. In this model >.82, favors surgical decompression management over medical management.

This model aims to synthesize current knowledge, but may fail to acknowledge the influence of real life factors, such as cost of care associated with a particular treatment strategy. These analyses required estimating values to achieve a reasonable efficacy estimate. The results reflect the limitations of the methods by which these values were obtained; the study is therefore limited by the uncertainty associated with utility values, probabilities, and complication rates. This uncertainty, however, was addressed with the sensitivity analyses; within the assumptions tested, the decision tree results are robust. Other limitations to this model include the lack of a randomized, prospective, controlled trial of surgery, limited decompression surgery performance, the assumed patient compliance of either therapy, patient symptom duration variability, or the (assumed) demographically varied sample populations across studies from which data was obtained. However, based on the available evidence from the literature, this model demonstrates the advantage of decompression surgery for treatment of patients with diabetic neuropathy and superimposed lower extremity nerve chronic nerve compressions. A recent review of the surgical literature has concluded "neurolysis significantly improves outcomes for diabetics with compressed nerves in the lower extremities" [25]. And, is supported by prospective results illustrating prevention at 18 months of any ulceraction or recurrence, as well as no amputations or wound infections as well [26], as well as an extended 5 year follow up cohort [26]; further lending support to the conclusion of the present study.

Acknowledgment

The authors would like to thank Dr. Whalen for editorial input.

References

1. Centres for Disease Control and Prevention (2011) Number of Americans with Diabetes Rises to Nearly 26 Million.
2. Wild S, Roglic G, Green A, Sicree R, King H (2004) Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 27: 1047-1053.
3. Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, et al. (1993) The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study. Neurology 43: 817-824.
4. Dyck PJ, Albers JW, Andersen H, Arezzo JC, Biessels GJ, et al. (2011) Diabetic Polyneuropathies: Update on Research Definition, Diagnostic Criteria and Estimation of Severity. Diabetes Metab Res Rev.
5. Leung PC (2007) Diabetic foot ulcers--a comprehensive review. Surgeon 5: 219-231.
6. Dellon AL (2008) The Dellon approach to neurolysis in the neuropathy patient with chronic nerve compression. Handchir Mikrochir Plast Chir 40: 351-360.
7. Chaudhry V, Russell J, Belzberg A (2008) Decompressive surgery of lower limbs for symmetrical diabetic peripheral neuropathy. Cochrane Database Syst Rev: CD006152.
8. Driver VR, Fabbi M, Lavery LA, Gibbons G (2010) The costs of diabetic foot: the economic case for the limb salvage team. J Vasc Surg 52: 17S-22S.
9. Aszmann OC, Kress KM, Dellon AL (2000) Results of decompression of peripheral nerves in diabetics: a prospective, blinded study. Plast Reconstr Surg 106: 816-822.
10. Aszmann O, Tassler PL, Dellon AL (2004) Changing the natural history of diabetic neuropathy: incidence of ulcer/amputation in the contra lateral limb of patients with a unilateral nerve decompression procedure. Ann Plast Surg 53: 517-522.
11. Biddinger KR, Amend KJ (2004) The role of surgical decompression for diabetic neuropathy. Foot Ankle Clin 9: 239-254.
12. Dellon AL (1992) Treatment of symptomatic diabetic neuropathy by surgical decompression of multiple peripheral nerves. Plast Reconstr Surg 89: 689-697.

13. Dellon AL (2007) Neurosurgical prevention of ulceration and amputation by decompression of lower extremity peripheral nerves in diabetic neuropathy: update 2006. Acta Neurochir Suppl 100: 149-151.

14. Dellon AL (2004) Diabetic neuropathy: review of a surgical approach to restore sensation, relieve pain, and prevent ulceration and amputation. Foot Ankle Int 25: 749-755.

15. Melenhorst WB, Overgoor ML, Gonera EG, Tellier MA, Houpt P (2009) Nerve decompression surgery as treatment for peripheral diabetic neuropathy: literature overview and awareness among medical professionals. Ann Plast Surg 63: 217-221.

16. Vinik A, Mehrabyan A, Colen L, Boulton A (2004) Focal entrapment neuropathies in diabetes. Diabetes Care 27: 1783-1788.

17. Hashemi SS, Cheikh I, Dellon AL (2013) Prevalence of Upper and Lower Extremity Tinel Signs in Diabetics: Crosssectional Study from a United States, Urban Hospital-based Population. J Diabetes Metab 4: 3.

18. Manchikanti L, Boswell MV, Manchukonda R, Cash KA, Giordano J (2008) Influence of prior opioid exposure on diagnostic facet joint nerve blocks. J Opioid Manag 4: 351-360.

19. Dellon AL, Muse VL, Nickerson DS, Akre T, Anderson SR, et al. (2012) Prevention of ulceration, amputation, and reduction of hospitalization: outcomes of a prospective multicenter trial of tibial neurolysis in patients with diabetic neuropathy. J Reconstr Microsurg 28: 241-246.

20. Nickerson DS (2010) Low recurrence rate of diabetic foot ulcer after nerve decompression. J Am Podiatr Med Assoc 100: 111-115.

21. Redekop WK, Stolk EA, Kok E, Lovas K, Kalo Z, et al. (2004) Diabetic foot ulcers and amputations: estimates of health utility for use in cost-effectiveness analyses of new treatments. Diabetes Metab 30: 549-556.

22. Torrance GW (1986) Measurement of health state utilities for economic appraisal. J Health Econ 5: 1-30.

23. Martin CL, Albers J, Herman WH, Cleary P, Waberski B, et al. (2006) Neuropathy among the diabetes control and complications trial cohort 8 years after trial completion. Diabetes Care 29: 340-344.

24. Dellon AL, Mackinnon SE, Seiler WA 4th (1988) Susceptibility of the diabetic nerve to chronic compression. Ann Plast Surg 20: 117-119.

25. Baltodano P, Bagdak B, Baile CR, Baez MJL, Tong A, et al. (2013) The Positive Effect of Neurolysis on Diabetic Patients with Compressed Nerves of the Lower Extremities: A Systematic Review and Meta-analysis. Plast Reconstr Surg Glob Open 1: e24.

26. Zhang W, Zhong W, Yang M, Shi J, Guowei L, et al. (2013) Evaluation of the clinical efficacy of multiple lower-extremity nerve decompression in diabetic peripheral neuropathy. Br J Neurosurg 27: 795-799.