SURGICAL PERIPHERAL NERVE DECOMPRESSION

For Treatment of Diabetic Neuropathy in the Foot

A Randomized Control Trial

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Conflict of Interest

- Nothing to disclose

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Surgical Peripheral Nerve Decompression

- Physicians' Services Incorporated Foundation provided grant funding

- This trial was registered with www.ClinicalTrials.gov and the registry number is NCT01006915
- Approved by the Combined Research Ethics Committee of Sault Ste. Marie, and the NOSM/Laurentian University Ethics Review Board

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Canadian Diabetes Mellitus Data

- Population of Canada: 2011 33,476,688
  2014 35,851,800

Growth of 2,374,31 27.09% **2.4% per year**

- Diabetes in Canada: 2011 1,793,352
  2014 2,011,347

Growth of 217,995 12.16% **4.1 % per year**

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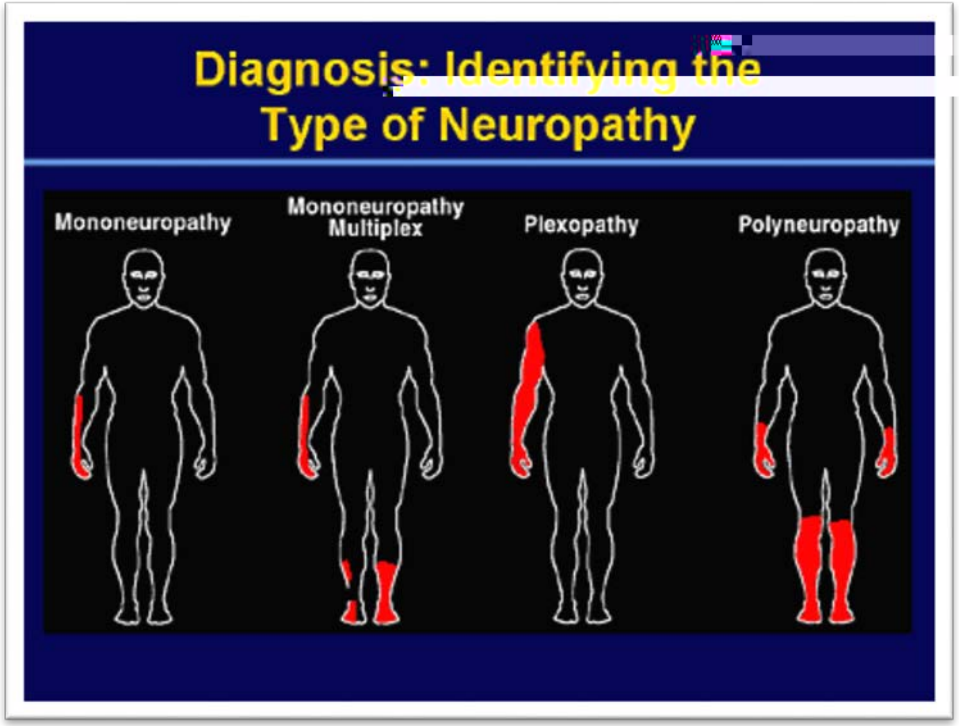
Background: Diabetic Peripheral Neuropathy

- Diabetic peripheral neuropathy a major contributor:
  - Foot ulcerations
  - Infections
  - Prolonged medical treatment
  - Amputation of the lower limb

- Pain and disability
- Large economic burden to healthcare system

Background: Peripheral Neuropathy

- A symmetrical, length-dependent sensorimotor polyneuropathy attributable to metabolic and microvessel alterations
- Symmetric Glove and Stocking Distribution



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Symptoms of Diabetic Neuropathy

- Sensory
  - Increased sensory symptoms (numbness, paresthesias, burning, prickling, allodynia)
  - Decreased tactile sensation (pinprick sensitivity, vibration, temperature)
- Motor
  - Weakness, atrophy, decreased ankle jerk reflex
- Autonomic
  - Anhydrosis, abnormal temperature regulation

Theory Behind Surgical Decompression

- "Double Crush" or "Double Pathology Hypothesis"
  - 1st insult: metabolic stress
  - 2nd insult: physical compression
- Diabetic nerves are significantly larger in size and less resistant to physical compression than their non diabetic counterpart (Riazi, Bril, et. al. *Diabetes Care* 2012)
- Therefore, if we can remove the 2nd insult by decompressing the diabetic nerve, the patient may experience a decrease in symptoms and an improved quality of life

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Existing Evidence

- Several published reports claim that surgical decompression of the major lower limb nerves (common peroneal nerve, deep peroneal nerve, tibial nerve):
  1. Decreases symptoms (i.e. pain, numbness)
  2. Decreases development of ulcers, related complications
- Existing evidence, although encouraging, is limited to Level IV and V
  - Non blinded
  - Non randomized

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Need for More Research

- **American Academy of Neurology Practice Advisory** recommended
  - *"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." - 2006*
- **The American Diabetes Association** asserted
  - *"We strongly support trials to determine whether these surgical procedures are beneficial." - 2007*

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An important observation is that few patients have complete relief of painful symptoms with any treatment, and that a **30% to 50% reduction in baseline pain** is considered to be a clinically meaningful response.

V. Bril J. England G.M. Franklin Evidence-based guideline: treatment of painful diabetic neuropathy: report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation Neurology:3 2011 1-21

Purpose

- To determine whether or not peripheral nerve decompression surgery is effective in the treatment of diabetic peripheral sensorimotor polyneuropathy

- **Null hypothesis:**
  - *surgical decompression of the common peroneal, deep peroneal, and tibial nerves has no benefit in ameliorating the symptoms of diabetic peripheral sensorimotor polyneuropathy*

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Design: RCT

- Randomized Control Trial; Single Blinded
- Control Group
  - Non surgical group
  - Subjects randomized to the control group continued to receive standard diabetic neuropathy care through the Algoma Diabetes Education Center
- Treatment Group
  - Patients underwent surgical decompression of their common peroneal, tibial, and deep peroneal nerves by Dr. Best
  - Also continued to receive standard diabetic neuropathy care through the Algoma Diabetes Education Center

Methods

Inclusion Criteria

1. Age >18 years
2. Presence of Type 1 or 2 diabetes mellitus (fasting plasma glucose > 7 mmol/L or casual plasma glucose > 11.1 mmol/L and symptoms of diabetes or a 2hr plasma glucose in a 75g oral glucose tolerance test > 11.1 mmol/L).(CanJDiab 2003)
3. Symptoms of paresthesias (including burning pain) or numbness present symmetrically in both feet, determined to be on a peripheral nerve basis.
4. Total Neuropathy Score of ≥ 2 based on symptoms, signs, and nerve conduction study abnormality.
5. Average pain on Likert scale (range 0 - 10) ≥5
6. Good diabetic control with Hgb A1C < 8.
7. Presence of Tinel's sign at the Tarsal Tunnel.
8. Possession of valid Ontario Hospital Insurance Plan (OHIP) coverage

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Methods

Exclusion Criteria

1. Other types of diabetes mellitus (gestational, drug-induced, etc.).
2. Other cause of neuropathy than diabetes such as vasculitis, amyloidosis, toxic neuropathy, HIV, renal failure, alcohol abuse, etc. Pure entrapment neuropathy without evidence of DSP.
3. Symptomatic lumbosacral spine disease.
4. Symptomatic lower extremity vascular disease.
5. Previous foot ulceration or amputation. Other contraindications to surgery such as significant ankle edema, venous stasis, morbid obesity, or previous surgery/injury which would be incompatible with appropriate wound healing.
6. History of Peripheral Arterial Disease
7. HbA1c > 8.1
8. Adults lacking capacity to consent, pregnant women, prisoners, non-English speakers who require an interpreter, and those unwilling or unable to participate in the full study follow-up.

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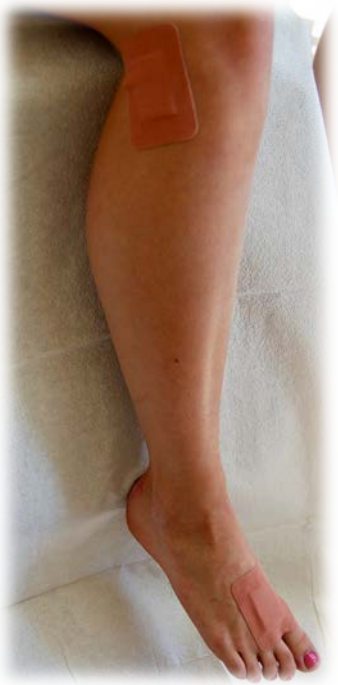
Methods: Evaluation

- Subjects in both the Control and Treatment Groups underwent evaluations at 0, 3, 6, and 12 months by blinded observers
- All patients coached not to reveal to assessors what group they were in; all patients wore identical opaque bandaging over standard incision site regardless if they had surgery or not



Time (months)	0	3	6	12
Symptoms	◊	◊	◊	◊
Signs	◊	◊	◊	◊
PSSD measurements	◊			◊
Nerve conduction studies	◊			◊
QoL/pain questionnaires	◊	◊	◊	◊

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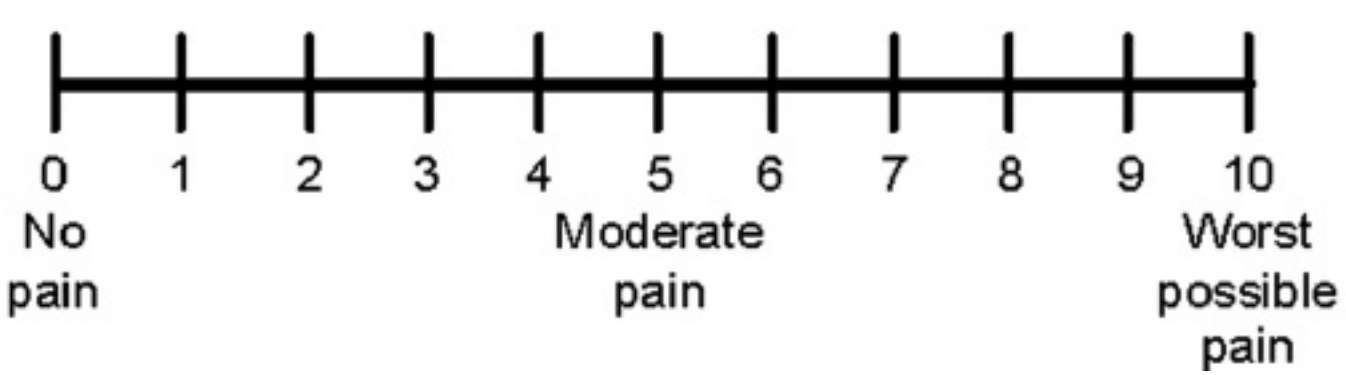
Evaluation: Pain

- The primary outcome parameter was improvement of pain using the 11-point Likert scale
- 0, no pain; 10, worst possible pain



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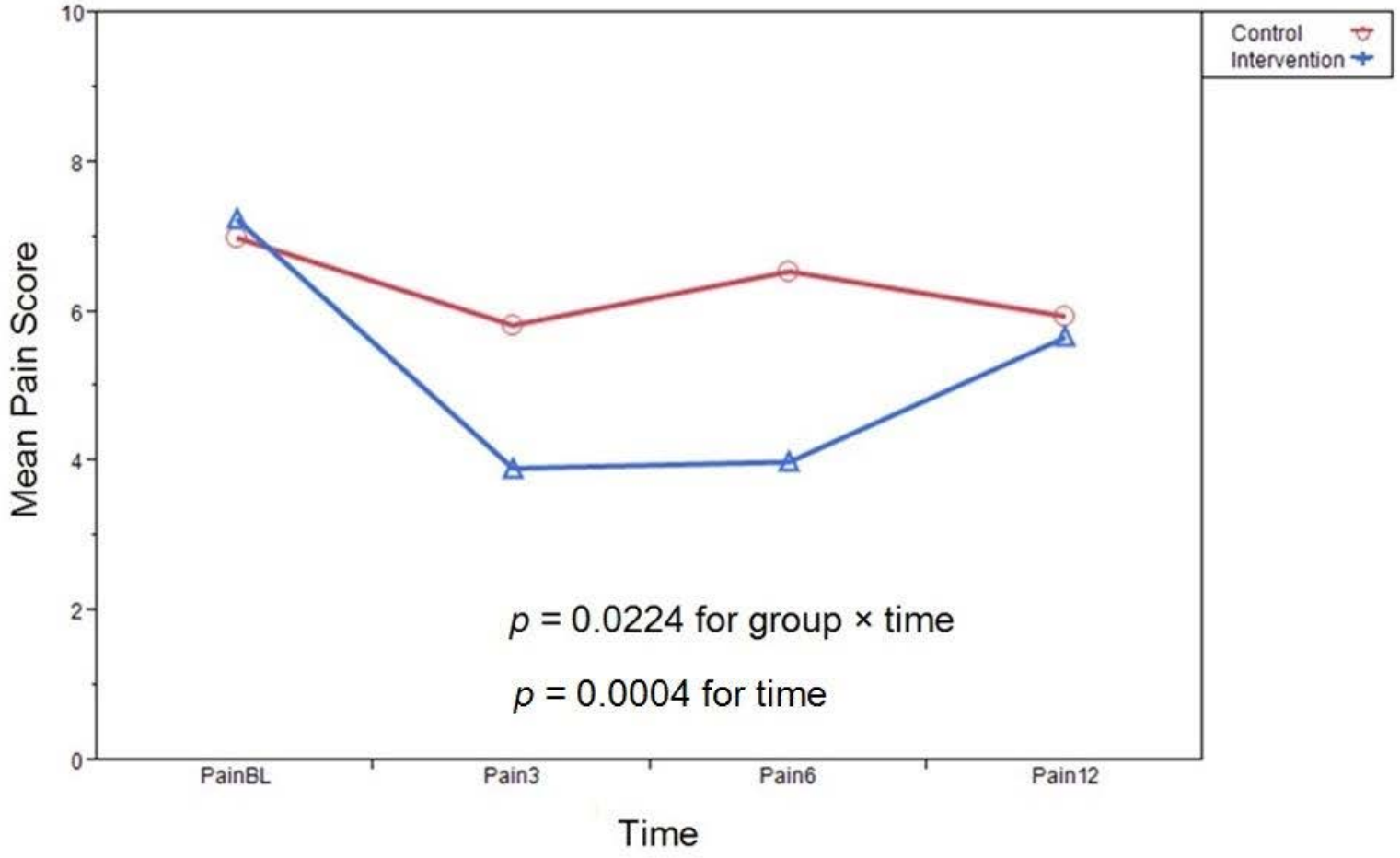
Pain Score Results: MANOVA



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Imputed Repeated Measures Analysis
(*n* = 22)

- Comparing pain scores vertically on graph at each time point:
  - *p* = 0.1617 = no differences in pain score **between** the groups over individual time points
- Comparing pain scores horizontally on graph:
  - *p*-value for time = **0.0004** = there is a significant difference in scores **within** groups across time
- Interaction term → joint effect of time and group:
  - *p*-value for group × time (interaction factor) = **0.0224 =** the two groups significantly differ in their **pain scores over time**

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Evaluation: Pain

Short-Form McGill Pain Questionnaire

Short-Form McGill Pain Questionnaire

PATIENT'S NAME: _____ DATE: _____

	NONE	MILD	MODERATE	SEVERE
THROBBING	0) _____	1) _____	2) _____	3) _____
SHOOTING	0) _____	1) _____	2) _____	3) _____
STABBING	0) _____	1) _____	2) _____	3) _____
SHARP	0) _____	1) _____	2) _____	3) _____
CRAMPING	0) _____	1) _____	2) _____	3) _____
GNAWING	0) _____	1) _____	2) _____	3) _____
HOT/BURNING	0) _____	1) _____	2) _____	3) _____
ACHING	0) _____	1) _____	2) _____	3) _____
HEAVY	0) _____	1) _____	2) _____	3) _____
TENDER	0) _____	1) _____	2) _____	3) _____
SPLITTING	0) _____	1) _____	2) _____	3) _____
TIRING/EXHAUSTING	0) _____	1) _____	2) _____	3) _____
SICKENING	0) _____	1) _____	2) _____	3) _____
FEARFUL	0) _____	1) _____	2) _____	3) _____
PUNISHING/CRUEL	0) _____	1) _____	2) _____	3) _____

VAS NO PAIN ——— WORST POSSIBLE PAIN

PPI

0 NO PAIN _____
1 MILD _____
2 DISCOMFORTING _____
3 DISTRESSING _____
4 HORRIBLE _____
5 EXCRUCIATING _____

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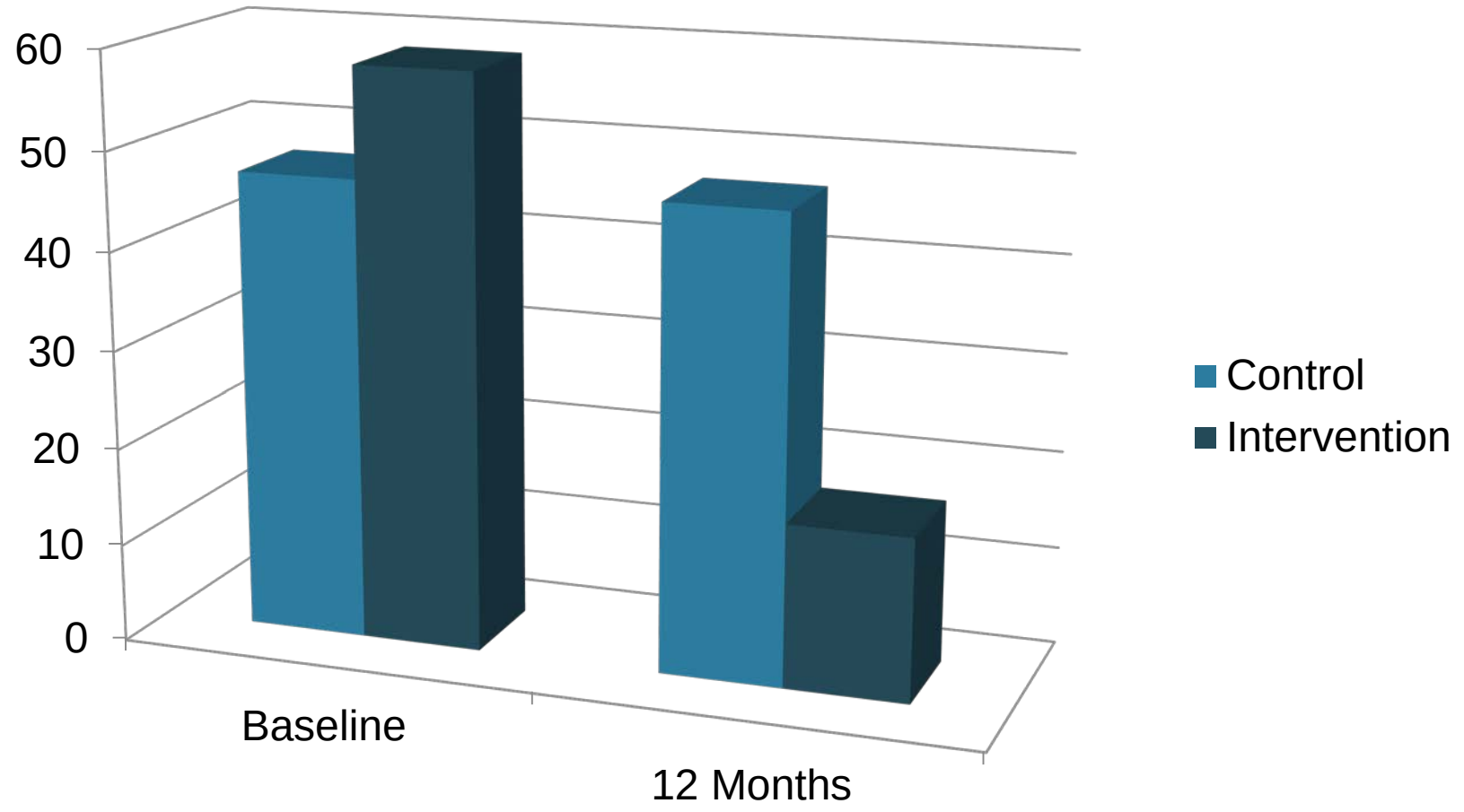
The short-form McGill Pain Questionnaire (SF-MPQ). Descriptors 1–11 represent the sensory dimension of pain experience and 12-15 represent the affective dimension. Each descriptor is ranked on an intensity scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe. The Present Pain Intensity (PPI) of the standard long-form McGill Pain Questionnaire (LF-MPQ) and the visual analogue scale (VAS) are also included to provide overall intensity scores.

Percent of McGill Pain Counts
Moderate to Severe



Evaluation: Quality of Life

- Neuro-QoL: a set of self-report measures that assesses the health-related quality of life (HRQOL) of adults and children with neurological disorders
- Northwestern University
- Validated
- Baseline, 3, 6, 12 months

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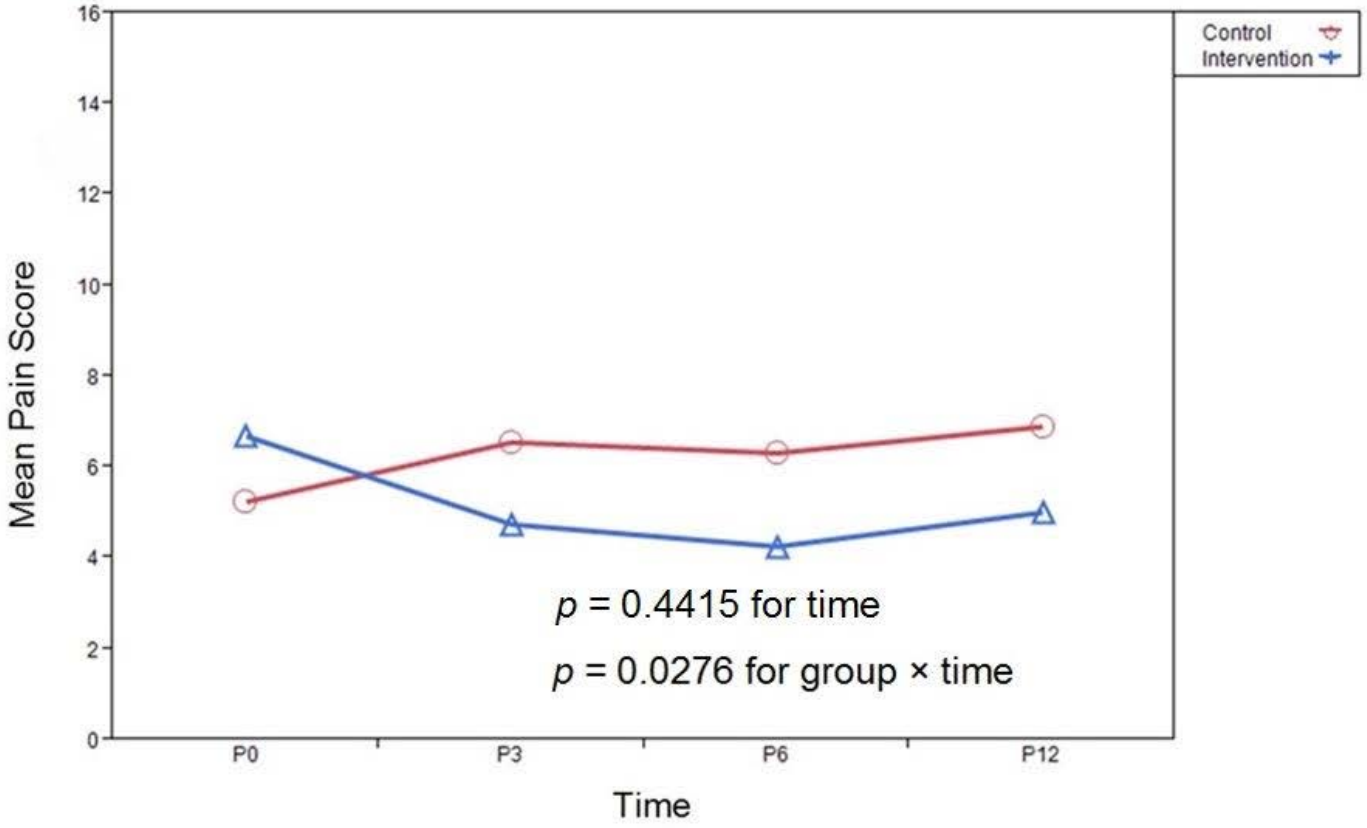
Pain QOL Results



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Analysis: Quality of Life (Neuro-QoL)

- **Pain**: significantly decreased at 12 months compared to baseline in the intervention group

- -3.33 (-5.67, -0.99), ***p* = 0.0079**

- No differences in other domains: Lost Feeling, Diffuse Sensory Motor Symptoms, Restriction in ADL, Disruption in Social Relationships, Emotional Distress, Neuropathy-specific Quality of Life, Overall Quality of Life

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Conclusions

- Our small sample size (n=22) prevented significant differences between groups at individual time points in pain scores
- However, when changes over time are taken into account within groups, **there are significant changes in pain scores for treatment group**
- When two groups are compared over time, **the average pain scores in the surgical group are significantly lower than the average pain scores in the control group**
- Pain domain of quality of life measures **significantly improved in treatment group**

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Conclusions

- Null hypothesis – disproven

- This pilot study is a validation through a single-blinded randomized control trial that **peripheral nerve decompression** for treatment of diabetic neuropathy of the lower limb is a viable treatment option to **reduce pain**

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Future Directions

Future Studies

- Multi-center, randomized control trial
- Increase sample size to increase power of the study
- Follow patients for longer period of time to see long term result past 12 months (i.e. 2 years)

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