Section: Medicine and Surgery

Original Research Article

APPLIED PHYSIOLOGY OF SURGICAL DECOMPRESSION IN DIABETIC NEUROPATHY: MICROANGIOPATHY, NEURAL COMPRESSION, AND LIMB SALVAGE

Ashraf Usman[1], Binny John[2], Ahammed Naseem V H[3], Ajitha B K[4]

[1]Assistant Professor, Department of Cardiovascular and Thoracic Surgery, Government Medical College, Thrissur (previously Assistant Professor, Government Medical College, Kottayam, Kerala, India
[2]Professor and Head of Department, Department of General Surgery, Government Medical College, Kottayam, Kerala, India
[3]Professor, Department of Physiology, Government Medical College, Wayanad, Kerala, India
[4]PhD Statistics, Department of Community Medicine, Government Medical College, Kozhikode, Kerala, India

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Corresponding Author:
Dr. Ahammed Naseem V H,
Email: naseemvh@gmail.com

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ABSTRACT

Background: Diabetic Peripheral Neuropathy is a multifactorial process that unites metabolic, vascular, and compressive mechanisms of injury. While the metabolic aspects of hyperglycemia and the vascular consequences of microangiopathy are well described, the mechanical contribution of nerve entrapment within fibro-osseous tunnels is often underappreciated. This entrapment aggravates ischemia, amplifies oxidative stress, and accelerates functional decline. **Materials and Methods:** The present work highlights the applied physiology of diabetic neuropathy with emphasis on microangiopathy, polyol pathway–driven nerve swelling, redox imbalance, and the particular vulnerability of autonomic fibers distributed peripherally within the nerve fascicle. Sudomotor failure, vasomotor dysregulation, and ischemia of the vasa nervorum are central events that converge to create an environment of progressive nerve dysfunction and tissue loss. Surgical decompression directly addresses these pathophysiological bottlenecks by restoring perfusion, relieving endoneurial hypoxia, and re-establishing physiological balance. **Result:** Two representative clinical photographs — one showing sequential ulcer healing and another documenting recovery of a nearly gangrenous toe — illustrate the potential for functional restitution once pathophysiology is corrected. A supplementary Semmes–Weinstein monofilament (SWM) line chart further demonstrates objective recovery of protective sensation. **Conclusion:** Understanding these mechanisms reframes decompression surgery not as a technical act alone, but as an applied physiological intervention with direct implications for limb salvage.

INTRODUCTION

Diabetes mellitus is among the most pervasive chronic diseases worldwide, and neuropathy is one of its most disabling complications. Estimates suggest that nearly half of patients with long standing diabetes develop peripheral neuropathy of the lower limbs with pain, sensory loss, autonomic dysfunction, and ulceration constituting a spectrum of morbidity that can culminate in limb loss. Despite major advances in medical therapy and glycemic control, diabetic neuropathy remains largely progressive, reflecting the complex convergence of metabolic and vascular derangements.

Conventional teaching emphasizes distal symmetric polyneuropathy as an inevitable metabolic outcome. Yet, clinical observation reveals a more nuanced reality: sites of anatomical narrowing such as the tarsal tunnel, the fibular head, or the intermetatarsal spaces often act as focal points of exacerbation. Entrapment neuropathy, superimposed on already vulnerable nerves, accelerates symptom progression. Patients develop burning pain, loss of protective sensation, recurrent ulceration, and trophic skin changes, often disproportionate to glycemic indices alone.

Applied physiology provides the conceptual bridge between biochemical derangements and clinical outcomes. The polyol pathway converts excess glucose into sorbitol,[1,8] causing Schwann cell swelling and depletion of protective NADPH. Microangiopathy thickens endoneurial

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capillaries,[2,10] reducing perfusion. Autonomic fibers, located peripherally within nerve fascicles, succumb early to ischemia, leading to impaired sweat and blood-flow regulation.[2,9] The vasa nervorum, compressed within tight fibro-osseous tunnels, further amplifies ischemic stress.

Surgical decompression, traditionally viewed as a mechanical maneuver, can thus be reframed as a physiological intervention — one that relieves ischemia, restores microcirculatory flow, and permits redox balance to normalize.[3,4,6,9] This manuscript elaborates on the pathophysiological underpinnings of diabetic neuropathy with emphasis on microangiopathy and autonomic distribution, presenting decompression as a direct application of physiological correction.

MATERIALS AND METHODS

This article draws on retrospective clinical observations at Government Medical College, Kottayam, spanning 2010 to 2025. The primary cohort comprised diabetic patients with painful neuropathy and neuropathic ulcers of the lower limbs, all of whom underwent Peripheral Nerve Decompression at anatomically relevant sites. Assessment included pain scores, Semmes–Weinstein monofilament (SWM) testing, and Rydel–Seiffer vibration thresholds, alongside clinical photography for ulcer and tissue evolution.

For the purposes of this applied physiology report, emphasis is placed not on the statistical outcomes, which are detailed elsewhere, but on representative physiological correlates. Two clinical photographs illustrate ulcer healing and recovery of ischemic toe tissue. One additional SWM line chart, not published in parallel work, is included as supporting evidence of physiological recovery of sensation. Ethical clearance for the retrospective study was obtained in December 2024.

Pathophysiology Core

Microangiopathy and Endoneurial Hypoxia: Diabetic microangiopathy manifests as diffuse thickening of the capillary basement membrane, deposition of advanced glycation end-products (AGEs), and endothelial dysfunction. Within the nerve, this pathology directly impairs the vasa nervorum, diminishing nutritive perfusion and oxygen delivery.[2,10] Capillaries that once adjusted to metabolic demand lose their autoregulatory capacity; nitric oxide availability falls, while endothelin-1 levels rise, fostering vasoconstriction.

The endoneurium, normally maintained in a state of low-pressure homeostasis, becomes hypoxic. Chronic hypoxia alters axonal metabolism, slows conduction velocity, and compromises Schwann cell integrity. Clinically, this presents as gradual sensory dulling, delayed wound healing, and the paradox of normal proximal pulses with distal ischemia. Microangiopathy is thus not merely a background phenomenon but a primary contributor to the vulnerability of diabetic nerves.

Polyol Pathway and Nerve Swelling: Excess glucose is diverted into the polyol pathway via aldose reductase, generating sorbitol[1,8]. Because sorbitol poorly traverses cell membranes, it accumulates within Schwann cells and axons, producing osmotic stress and cellular swelling. This swelling is not benign: it narrows endoneurial spaces, increases intrafascicular pressure, and heightens susceptibility to external compression at anatomical tunnels.

The metabolic consequences are equally severe. Sorbitol generation consumes NADPH, a cofactor also required for regenerating reduced glutathione — the primary antioxidant defense. As NADPH is diverted, glutathione reserves diminish, leaving the nerve vulnerable to oxidative stress.[1,5] Concurrently, decreased NAD^+ availability impairs glycolysis and mitochondrial respiration, starving the axon of energy.

This triad — swelling, redox vulnerability, and energy deficiency — renders the diabetic nerve structurally tense and metabolically exhausted, a substrate primed for failure under compressive stress.

Redox Imbalance and Oxidative Stress

Hyperglycemia drives mitochondrial overproduction of reactive oxygen species (ROS), overwhelming antioxidant defenses. Coupled with the NADPH depletion of the polyol pathway, this creates a persistent redox imbalance.[1,5] ROS damage lipids, proteins, and DNA within the nerve, impairing ion channel function and slowing axonal conduction.

The interaction between oxidative stress and AGEs is particularly destructive. Cross-linked collagen stiffens peri- and epineural tissues, reducing the compliance of fibro-osseous tunnels. Thus, oxidative stress not only damages nerves intrinsically but also alter the mechanical milieu, locking swollen nerves into rigid tunnels.

Clinically, this translates into refractory pain, sensitivity to minor trauma, and heightened risk of ulceration. Importantly, redox imbalance is not fully ***corrected by glycemic control alone; decompression contributes by reducing local hypoxia and oxidative flux.***

Autonomic Fiber Distribution and Early Dysfunction

Autonomic fibers — both sudomotor and vasomotor — are located peripherally within nerve fascicles.[2,9] This anatomical arrangement, advantageous for rapid signaling under normal physiology, makes them first targets of hypoxia and compression.

Sudomotor dysfunction arises early. With impaired sweat gland innervation, the skin becomes dry, cracked, and prone to fissuring. Loss of the hydrolipidic film weakens the protective barrier, allowing microbial invasion and ulcer formation.

Vasomotor dysfunction compounds the problem. Loss of finely tuned vasoconstrictor and dilator control results in inappropriate arteriovenous shunting. Nutrient capillaries remain under perfused even as global limb blood flow appears intact.

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Clinically, the paradox is striking: palpable pulses coexist with ischemic, non-healing ulcers.

Because autonomic fibers precede large fiber loss, their dysfunction is an early clinical sign — cold feet, dry skin, color changes — that the underlying pathophysiology is advancing. Their peripheral fascicular position also explains why decompression can produce rapid improvement in tissue texture and perfusion once space and oxygen are restored.

Ischemia of the Vasa Nervorum

The vasa nervorum are delicate vessels supplying peripheral nerves. In diabetes, they are doubly compromised both intrinsically by microangiopathy and extrinsically by tunnel entrapment. Anatomical bottlenecks such as the tarsal tunnel or fibular neck exert pressure that collapses these already diseased vessels.

The result is a vicious cycle wherein ischemia impairs axonal transport, which further increases intraneural edema, which in turn worsens compression. Entrapment neuropathy in the diabetic patient is therefore not incidental but pathognomonic of compounded injury.[6,7]

Decompression breaks this cycle.[3,4,6,9] By releasing the rigid fibro-osseous confines, the vasa nervorum can reperfuse, intraneural pressure declines, and endoneurial oxygen tension rises. The clinical correlate is rapid pain relief and, in many cases, visible improvement in skin color and temperature within days.

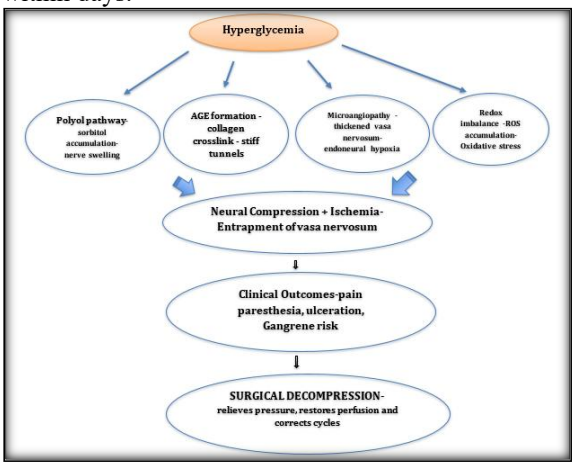

Figure 1: Pathophysiological cycles in diabetic neuropathy. Hyperglycemia initiates multiple processes — polyol pathway activation, advanced glycation end-product (AGE) formation, and microangiopathy with redox imbalance. These converge on a final common pathway of intraneural edema, ion channel dysfunction, and ischemia of the vasa nervorum. The result is pain, sensory loss, ulceration, and risk of gangrene. Surgical decompression interrupts this cycle by relieving pressure and restoring perfusion.

RESULT

The clinical manifestations of diabetic neuropathy mirror the underlying physiological insults. Pain, numbness, and burning dysesthesia correspond to early small fiber and autonomic dysfunction, while loss of vibration and protective sensation represent later large fiber involvement.

Pain and Dysesthesia. Patients describe burning, stabbing, or electric sensations in the feet, often worse at night. This corresponds to early ischemia of small fibers and persistent oxidative stress at the fascicular periphery. The paradox is that pain often intensifies before loss of sensation, highlighting that hyperexcitable but ischemic fibers can coexist with declining function.

Loss of Protective Sensation. As the disease progresses, Semmes–Weinstein monofilament (SWM) testing and vibration threshold assessments reveal loss of protective sensation. Patients become vulnerable to unnoticed trauma from footwear, uneven surfaces, or thermal injury. The physiology is clear in that swollen axons, reduced axoplasmic transport, and ischemic demyelination blunt afferent signaling.

Ulcer Formation. The combined failure of sudomotor secretion and vasomotor regulation creates the perfect storm for ulceration. Dry, fissured skin allows microbial ingress, while poor capillary perfusion impairs healing. Even when proximal pulses remain strong, distal ischemia from arteriovenous shunting and microangiopathy arrests tissue repair.

Limb Salvage: These processes culminate in the most feared complication — limb-threatening ulcer or gangrene. Yet, surgical decompression alters this trajectory. Restoration of vasa nervorum flow and reduction of endoneurial pressure improve sudomotor activity, restore skin pliability, and enhance capillary perfusion. The clinical reality is striking in that ischemic tissue may regain warmth and color, and ulcers that resisted conservative care may close within weeks.

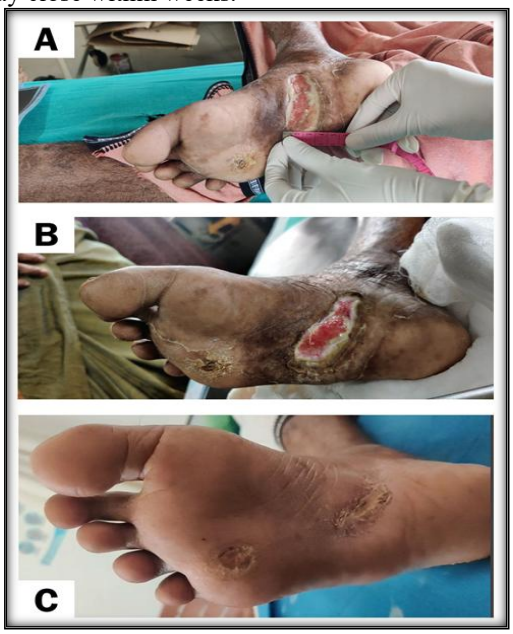

Figure 2: Sequential healing of a Wagner-2 plantar ulcer following surgical decompression. Baseline pre operative ulcer (A), partial closure at 5 weeks (B), and complete healing by 20 weeks (C). Healing corresponds with restored sudomotor activity and improved local perfusion.

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Two representative cases illustrate this physiology in action: (1) a Wagner-2 plantar ulcer that healed within six weeks after decompression, and (2) a nearly gangrenous toe that regained function, texture, and viability following intervention.

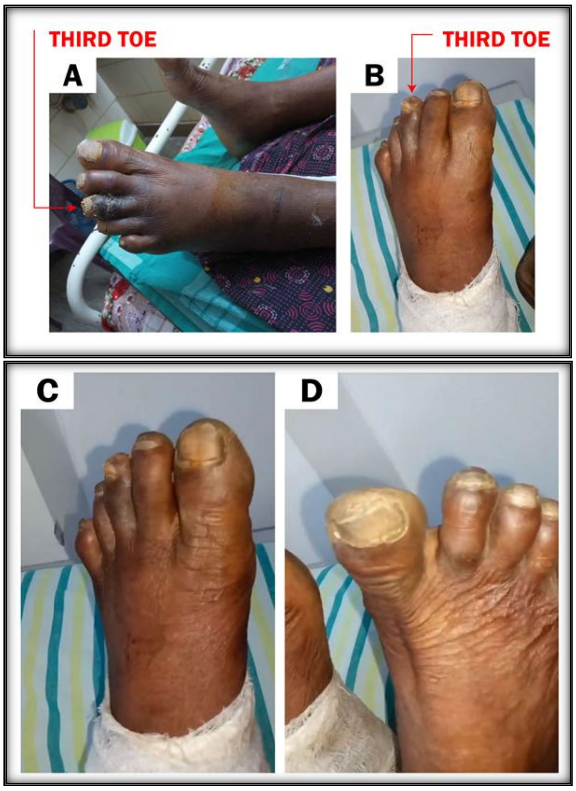

Figure 3: Recovery of a nearly gangrenous toe and improvement of the texture and function of the foot on the operated limb(A to D). Initial ischemic, discolored appearance (A) of the third toe contrasted with regained color, texture, and viability at follow-up (B). C and D demonstrate comparative features of the feet on the operated (bandaged) and non-operated limbs. Note the nail and toe texture of the unoperated foot compared to the operated foot. The operated limb regained its vitality demonstrating reversal of vasa nervorum ischemia and autonomic dysfunction.

These visual narratives embody the applied physiology that bridges theory and outcome.

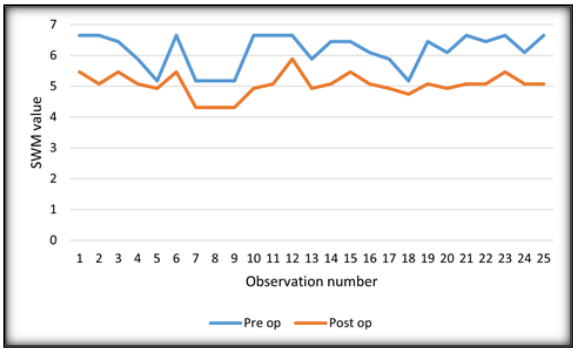

Figure 4: Semmes–Weinstein monofilament (SWM) line chart illustrating recovery of protective sensation after decompression. Progressive shift toward lower thresholds (≤5.07) reflects restoration of large fiber function in parallel with physiological correction.

DISCUSSION

The applied physiology of diabetic neuropathy demonstrates that the condition is not a static, irreversible degeneration, but a dynamic interplay of metabolic, vascular, and mechanical insults. This distinction reframes our therapeutic approach.

Integration of Pathways.

- The polyol pathway induces osmotic nerve swelling and redox vulnerability.
- Microangiopathy restricts nutritive perfusion, producing endoneurial hypoxia.
- Oxidative stress stiffens connective tissues and injures axonal proteins.
- Autonomic fiber distribution predisposes to early dysfunction in sweat and vascular control.
- Vasa nervorum ischemia, worsened by anatomical compression, creates a bottleneck that no pharmacological agent can directly relieve.

These insults converge, not in isolation but synergistically. A swollen, hypoxic, oxidatively stressed nerve trapped in a rigid tunnel cannot recover, regardless of glycemic control alone.

Role of Decompression. Surgical decompression interrupts this cycle. By releasing fibro-osseous tunnels, intraneural pressure falls, vasa nervorum perfusion improves, and oxidative stress is mitigated. Within days, patients often report diminished pain and improved warmth — clinical correlates of restored physiology. Over weeks, objective tests such as SWM confirm regained protective sensation.

It is crucial to recognize that decompression is not merely mechanical. Its true value lies in correcting the physiological environment:

- Relieving hypoxia,
- Allowing axonal transport to resume,
- Supporting mitochondrial recovery,
- Restoring autonomic balance.

Distinct from Medical Therapy. Glycemic control, antioxidants, and vasodilators address metabolic and vascular contributors but cannot eliminate localized compression. Similarly, footwear and offloading prevent further trauma but do not restore nerve physiology. Decompression uniquely targets the mechanical bottleneck that aggravates all other pathophysiological insults.

Clinical Implications. Recognition of diabetic neuropathy as a reversible physiological disorder at certain stages has profound implications. It suggests that early identification of patients with pain, sudomotor failure, or focal entrapment signs should prompt consideration of decompression before irreversible axonal death occurs.

The photographs presented here underscore this principle. The recovery of a nearly gangrenous toe and the closure of a neuropathic ulcer demonstrate that what once was considered inevitable progression can be reversed if physiology is restored.

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CONCLUSION

Diabetic neuropathy represents the convergence of polyol pathway stress, microangiopathy, oxidative imbalance, and mechanical entrapment. Autonomic dysfunction and ischemia of the vasa nervorum are early and pivotal events that herald progression toward ulceration and limb loss.

Surgical decompression directly addresses this complex physiology. By relieving tunnel pressure, restoring vasa nervorum perfusion and reducing oxidative flux, decompression re-establishes the conditions necessary for nerve recovery. The clinical correlates — pain relief, return of protective sensation, and ulcer healing — are not mere outcomes, but demonstrations of applied physiology in action.

This recognition reframes decompression as a physiological correction rather than a purely surgical act. Diabetic neuropathy, though progressive, is reversible in defined stages, and timely intervention can salvage both limb and function.

REFERENCES

1. Yang Y, Zhao B, Wang Y, Lan H, Liu X, Hu Y, et al. Diabetic neuropathy: cutting-edge research and future directions. Signal Transduct Target Ther. 2025;10:63.
2. Fang F, Bai Y, Zhang Q, Chen H, Wang C, Zhang Y, et al. Microangiopathy in diabetic polyneuropathy revisited. Diabetologia. 2018;61(6):1349-59.
3. Ma F, Wang G, Wu Y, Xie B, Zhang W. Improving effects of peripheral nerve decompression microsurgery of lower limbs in patients with diabetic peripheral neuropathy. Brain Sci. 2023;13(4):558.
4. Liao C, Zhang Y, Chen L. Nerve decompression for diabetic peripheral neuropathy with nerve entrapment: a narrative review. Front Endocrinol (Lausanne). 2024;15:1147538.
5. Fischer D, Henningsen H, Scherer SS, et al. Exploring structural and molecular features of sciatic nerve lesions in diabetic nerve damage. Diabetes. 2024;74(1):65-78.
6. Dellon AL. Nerve decompression in diabetics with chronic nerve compression. Plast Aesthet Res. 2022;9:13.
7. Daeschler SC, Pennekamp A, Tsilingiris D, Bursacovschi C, Harhaus L, et al. Effect of surgical release of entrapped peripheral nerves in sensorimotor diabetic neuropathy on pain and sensory dysfunction: study protocol of a prospective, controlled clinical trial. J Pers Med. 2023;13(2):348.
8. Wu L, Li Y, Wang H, et al. Diabetic peripheral neuropathy based on Schwann cell injury. Front Endocrinol (Lausanne). 2024;15:1427679.
9. Liao C, Zhang Y, He C, et al. Triple-nerve decompression surgery for the treatment of painful diabetic peripheral neuropathy: a randomized clinical trial. Front Neurol. 2022;13:1067346.
10. Li Y, Xu Z, Wang Y, et al. Diabetic vascular diseases: molecular mechanisms and therapeutic interventions. Signal Transduct Target Ther. 2023;8:400..

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