Morphometry of the sural nerve in diabetic neuropathy: a systematic review

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INTRODUCTION

Diabetic polyneuropathy (DPN), a complication of Diabetes Mellitus, affects up to 50% of diabetic patients. It can precipitate complications with high morbidities, such as foot ulceration, gangrene, and Charcot's joint (*Bodman et al, 2023*)

The **Sural nerve** is frequently affected due to length-dependent neuropathy. While nerve conduction study is the current gold standard for evaluation, it provides limited information about nerve morphology. Instead, **peripheral nerve ultrasonography** offers potential in evaluating peripheral neuropathies whilst being cheap, non-invasive and widely accessible (*Breiner et al, 2017*). This systematic review aims to establish normative and pathological **Cross-sectional area (CSA)** values of the sural nerve to differentiate DPN severity, contributing to early diagnosis and better prognosis. (*Arumugam et al, 2016*)

METHODOLOGY

A systematic search on Sural nerve CSA in normal and diabetic populations was conducted by reviewing published articles obtained from five major databases (*EMBASE, Cochrane, Scopus, PubMed, and Web of Science*) from 1 January 2015 to 23 June 2023. Relevant data was extracted and meta-analysis was conducted using Open Meta-Analyst software and R console based on a continuous random-effects model.

Heterogeneity assessment and subgroup analysis was then performed to calculate Cochran's Q and I2 values based on Cochrane guidelines. Finally, the Anatomical Quality Assessment (AQUA) tool was used to assess reliability of results.

RESULTS

STUDY SELECTION:

There were 30 studies reviewed that were selected from an initial pool of 217, with the information about 2901 sural nerves (2085 healthy, and 816 from diabetic patients) used for meta-analysis (Preferred Reporting Items for Systematic reviews and Meta-Analyses [PRISMA] flow chart *Fig 1*)

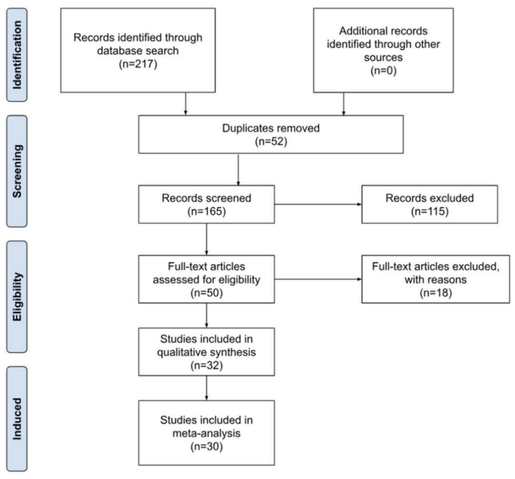

Fig 1: PRISMA flowchart of study selection

LANDMARKS:

The most common landmarks used for assessment were the:
(1) lateral malleolus;
(2) ankle; and
(3) lesser saphenous vein

MEAN SURAL NERVE CSA:

The study notes a statistically significant **increase in sural nerve CSA** in **patients with diabetic polyneuropathy (DPN)**, when compared to their peers in a healthy population, with a significant heterogeneity of 99.8% (I^2 > 95%) with a Cochrane Q statistic of P <0.001.

Ultrasonographic measurements showed that the pooled weight mean CSAs (at a 95% confidence interval) were **2.63 mm²** (*Fig* 3) and **3.19 mm²**. (*Fig* 2) The mean sural nerve CSA was larger in type 1 diabetes than type 2 diabetics, as well as the healthy population. The increase in weighted CSA between the type 1 and type 2 diabetic populations proved to be **statistically insignificant.**

OTHER VARIABLES INFLUENCING SURAL NERVE CSA:

The study also notes variations in sural nerve CSA with variance in geographical region, measurement sites/sides, age, height and weight, and BMI; however no significant difference in CSAs were noted based on the aforementioned measurement sites, nor between the left and right lower limbs.

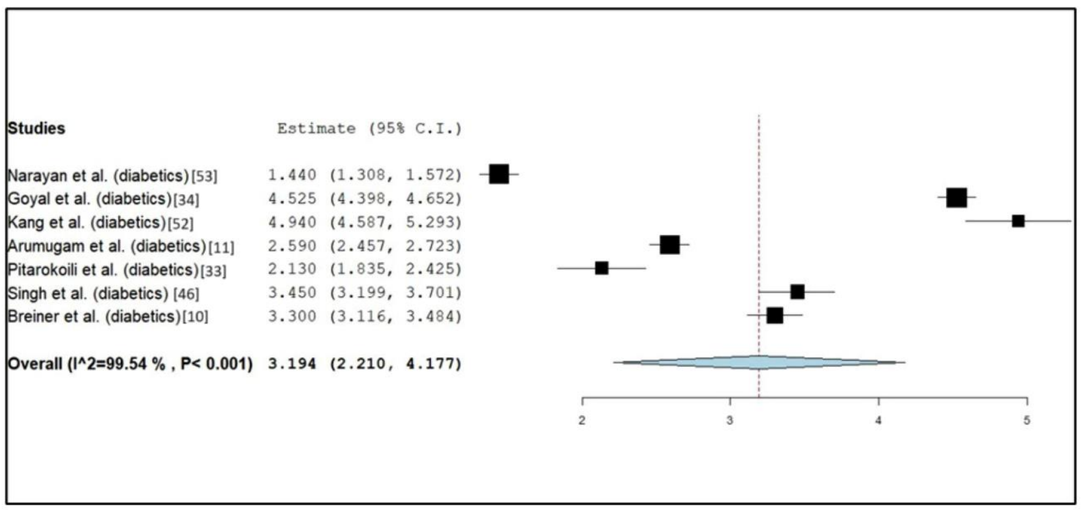

Fig 2: Forrest plot of reported estimate CSA of diabetic subjects

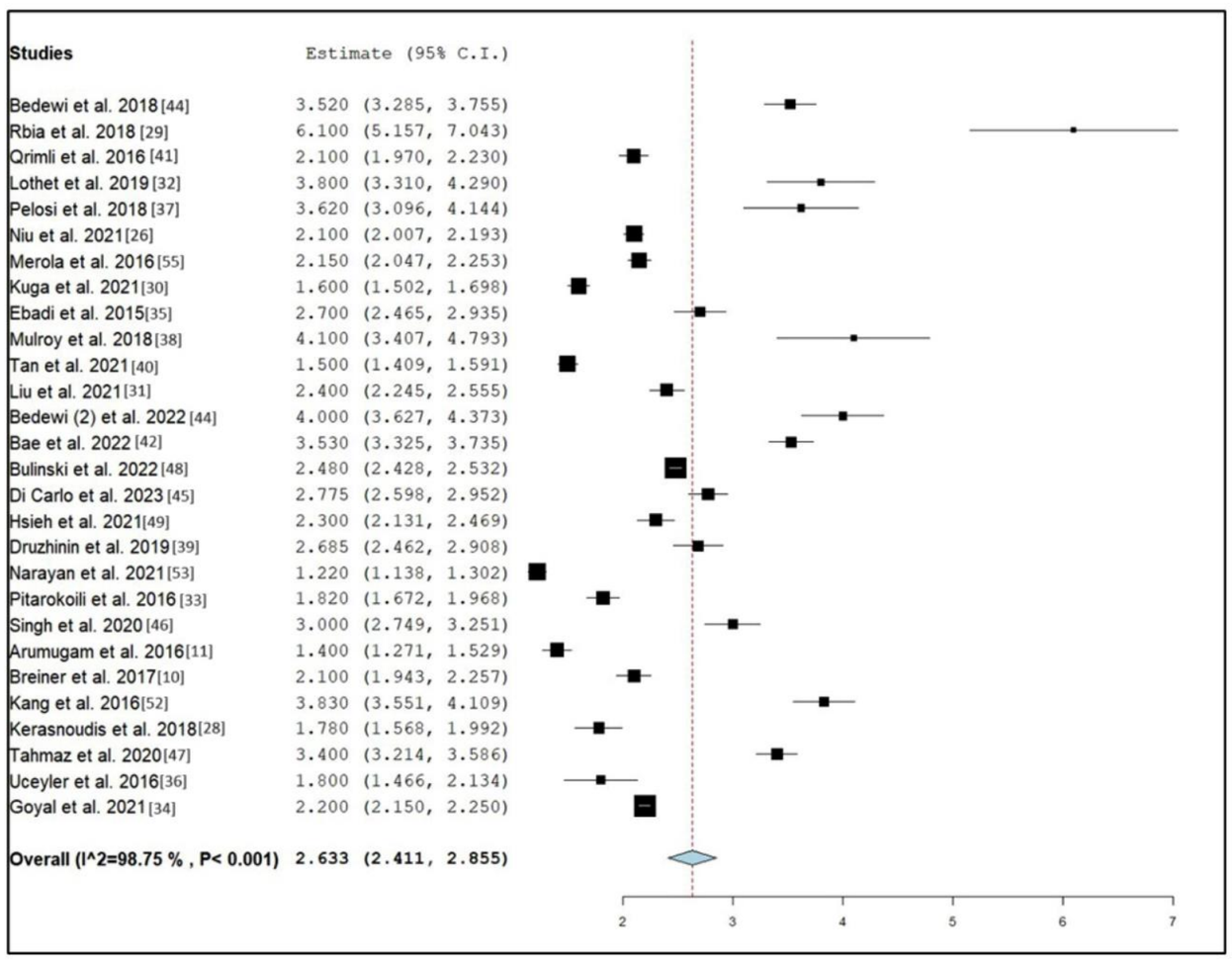

Fig 3: Forrest plot of reported estimate CSA of healthy subjects

DISCUSSION

Sural nerve CSAs vary greatly for healthy individuals and diabetic individuals without DPN, making its use in clinical diagnostics of diabetes itself less feasible.

Sural nerve CSAs have no significant difference between diabetic patients without DPN and healthy individuals, suggesting that **diabetes in isolation cannot be detected using ultrasonography** of nerve CSA.

DPN PATIENTS VERSUS HEALTHY INDIVIDUALS:

Sural Nerve CSAs have a significant difference between diabetic patients with diabetic polyneuropathy (DPN) compared to healthy individuals

- Highlights hypertrophic state of the sural nerve in DPN patients; raising the possibility of ultrasonography of nerve CSA as a tool to gauge development of DPN across time
- Constant nerve CSA monitoring during follow-up can help in identifying the relationship between DPN and sural nerve morphology

FUTURE STUDIES

More studies need to be done to identify other factors and confounding variables to be considered for diagnostic measurements

Some confounding variables include:
- Clinical factors: **leg dominance, years with diabetes, associated comorbidities; and**
- Demographic factors: **geographic regions, age, BMI**, which should be evaluated as well

- Relationship between body metrics and sural nerve CSA in healthy and diabetic populations in **different geographical regions**.