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# COMPARISON OF SURAL NERVE AMPLITUDE AND SURAL/ RADIAL AMPLITUDE RATIO IN ELECTRODIAGNOSIS OF PATIENTS WITH NEUROPATHY IN TYPE 2 DIABETES

**Shamsaei G.H[1], Zakerkish M. [2], Kashipazha D.[3], Moradi M.[4], Zakizadeh H.[5*]**

[1.] Department of Neurology, School of Medicine, Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

[2.] Department of Internal Medicine, School of Medicine, Diabetes Research Center, Health Research Institute, Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

[3.] Department of Neurology, School of Medicine, Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

[4.] School of Public Health, Ahvaz Jondishapour University of Medical Sciences, Ahvaz, Iran.

[5.] Department of Neurology, School of Medicine, Golestan Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

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***Abstract***

*Diabetic neuropathy is the most common and bothersome diabetes mellitus complication, leading to considerable morbidity and mortality. The results of these studies and the importance of early detection and prevention of polyneuropathy in diabetic patients motivated the authors to carry out the present study.*

*In this cross-sectional study all consecutive patients with type 2 diabetes mellitus were referred to the Endocrinology Clinic at Golestan Hospital in Ahvaz, Iran. The Nihon Kochden gadget was utilized on all patients, who were all examined by an individual. Average sensory amplitude was defined as greater than 6 V for the sural nerve and greater than 15 V for the radial nerve. In the present investigation, a sural/radial nerve amplitude ratio greater than or equal to 21 % was considered normal.*

*In total, 80 subjects were included in the analysis, there is a non-significant direct correlation between the sural nerve and sural/radial nerve amplitude ratio, to diagnose patients with and without neuropathy ($p=0.625$). Moreover, there is a non-significant direct correlation between the sural nerve and sural/radial nerve amplitude ratio with the body mass index of patients with diabetes, and this correlation is negligible ($p>0.05$).*

*The findings demonstrated that sural/radial nerve amplitude ratio was a promising method for detecting neuropathy in patients with type 2 diabetes. In addition,, sural nerve and sural/ radial nerve amplitude ratio had a significant inversion relationship with age and duration of diabetes for detecting diabetic neuropathy in type 2 diabetes patients.*

***Keywords:*** *peripheral neuropathy, diabetic neuropathy, diabetes mellitus, sural nerve, radial nerve.*

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***Address for Correspondence:***

Hossein Zakizadeh, MD
Department of Neurology Ahvaz Jundishapur University of Medical Sciences
Golestan Street, Ahvaz 6135715794, Iran
Tel.: +986133348320
E-mail: Hossein.zakizadeh20@gmail.com

### *INTRODUCTION*

Diabetic neuropathy is the most common and worrying complication of diabetes mellitus, resulting in significant morbidity and mortality. It has a significant financial burden for diabetes control [*Lontchi-Yimagou E et al., 2013*]. Up to 50% of patients are affected by diabetic neuropathy, resulting in higher morbidity and decreased quality of life [*García-Pérez L et al., 2013*]. Other diabetes complications require more hospitalizations than all diabetic neuropathy, accounting for 50 to 75% of non-traumatic amputations in developed nations [*Madanchi N et al., 2013*].

Although impaired glucose control appears to be a key component in diabetic neuropathy, it has a complex natural history and pathogenesis. Clinical syndromes that affect several parts of the nervous system, alone or in combination, constitute diabetic neuropathy [*Selvarajah D et al., 2019*]. Symptoms and signs that are generic and insidious with sluggish advancement may be similar to those observed in many different diseases, making it difficult to distinguish one from the other [*Yang H et al., 2019*]. Even when diabetic neuropathy is present, less than a third of doctors know the underlying reason or discuss it with their patients. Unfortunately, this is true for both endocrinologists and non-endocrinologists [*Dyck P et al., 1993; Albers J, Pop-Busui R, 2014*]. The metabolic syndrome, including pre-diabetes, has been linked to neuropathy by a growing body of research. Peripheral nerve damage in diabetes may cause entrapment, a common symptom. As a result of endoneuria ischemia and metabolic variables, the median nerve fibers are more prone to localized entrapment [*Suljic E, Drnda S, 2019; Jende J et al., 2022*].


*To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world*

Peripheral neuropathy is accurately diagnosed by measuring the amplitude of sensory nerve action potentials [*Zhang Y et al., 2014*]. Besides, the sural and radial sensory nerve action potentials are particularly beneficial in the electrodiagnosis of polyneuropathy since they are at low risk of compressive damage [*Guo Y et al., 2015*]. It is not difficult to diagnose axonal polyneuropathy in instances with subtle symptoms, especially if the electrophysiological data appear to be normal. Indeed, neurosensory conduction, particularly in the sural nerve, depends on the sensitivity and specificity of the axonal polyneuropathy measurement [*Rutkove S et al., 1997; Chung T et al., 2014*]. In other words, the natural fluctuations in a unit of sensorineural function potential are incredibly large in terms of age, weight, sex, and body mass index (BMI) [*Fujimaki Y et al., 2009*]. Several studies have justified using the sural/radial nerve amplitude ratio (SRAR) to improve the results [*Latov N, 2011; Dunnigan S et al., 2013*]. The sural/radial nerve amplitude ratio is more sensitive to degradation than any potential for pure sensory nerve function in diabetes or another axonal polyneuropathy [*Papanas N et al., 2010; Barnett C et al., 2012*]. Although sensory nerve function can be affected by various factors (i.e., BMI, age, and sex), some studies found that the SRAR was more impervious to these factors [*Sreenivasan A et al., 2016; Lai Y et al., 2020*]. Therefore, the present study has been performed on diabetic patients to compare two electrophysiological methods, including the SRAR and sensory nerve function potential. Also, the results of these studies and the importance of early detection and prevention of polyneuropathy in diabetic patients motivated the authors to carry out the present study.

### *MATERIAL AND METHODS*

***Study design and setting:*** The Ethics Committee of Ahvaz Jundishapur University of Medical Sciences accepted this cross-sectional study (*IR.AJUMS.HGOLESTAN.REC.1399.160*), and patients were then informed of the study procedure. All consecutive patients with type 2 diabetes mellitus were referred to the Endocrinology Clinic at Golestan Hospital in Ahvaz, Iran, from April to September 2021 for diabetes mellitus staging, with or without symptoms suggestive of polyneuropathy, were enrolled in the study based on American Diabetes Association criteria [*Chung W et al., 2020*].

Patients dissatisfied with the study, lack of clinical suspicion according to the Toronto standard [*Bril V et al., 2009*], and the concomitant presence of in-

herited or acquired neuropathies such as toxic or metabolic, use of neurotoxic drugs, alcoholism, and liver or kidney failure were excluded from this study.

***Electrophysiological methods:*** The Nihon Kochden gadget was utilized on all patients, who were all examined by an individual. Before the trial, all patients' hand and foot skin temperatures were tested, and if they were below 30°C, hot water was used to bring them to 30°C. Patients' sural and radial nerves' sensory amplitudes were assessed and recorded. 3 cm was always the distance between the active and reference electrodes. To assess the sural nerve amplitude ratio (SNAR), the stimulator was positioned 12 *cm* from the nerve and 10 *cm* from the radial nerve. The non-dominant hands and feet of patients were always chosen for amplitude recording. Average sensory amplitude was defined as greater than 6 *V* for the sural nerve and greater than 15 *V* for the radial nerve. In the present investigation, a SRAR greater than or equal to 21 percent was considered normal.

***Sample size:*** The sample size was calculated by a statistician using the following equation according to a similar article by Ying Guo and co-authors (2015).

$$n = \frac{(z - 0.5\alpha + z_1 - \beta)^2 \times [P_1(1 - P_1) + P_2(1-P_2)]}{d^2} = 79$$

***Statistical analysis:*** Frequency and percentage were used to describe qualitative variables. Mean and standard deviation, median, and interquartile range were used to describe quantitative variables. The correlation between quantitative variables was examined using the Spearman rank correlation coefficient. The correlation coefficient (r) was interpreted using the following cut-off points. The Mann-Whitney U test was used to compare quantitative variables between men and women. Utilizing the Shapiro-Wilk test, the normality of the data was determined. The kappa coefficient was utilized to evaluate the concordance between the sensory sural nerve amplitude and the sensory sural/radial nerve amplitude, and the following cut-off points were provided to interpret this coefficient. The McNemar's test compared the sensory amplitudes of the without neuropathy, sural, and the sural/radial nerve. $P<0.05$ was regarded as the statistical significance level, and SPSS 22v was used to analyze the data.

***Table 1.***

Descriptive information of the participants in the study.

| Variables | Patients (N = 80) |
|---|---|
| **Age (year),** Mean ± SD (Range) | 57.98 ± 8.85 (39 – 76) |
| **Duration of DM (year),** Mean ± SD (Range) | 9.27 ± 3.82 (1 – 20) |
| **BMI (kg/m²),** Mean ± SD (Range) | 29.98 ± 3.19 (24 – 36) |
| **Sensory domain** | |
| **of the sural nerve,** Mean ± SD (Range) | 4.46 ± 3.19 (1.1 – 21.5) |
| **of the radial nerve,** Mean ± SD (Range) | 24.31 ± 2.95 (12.7 –36.1) |
| **of the sural/radial nerve,** Mean ± SD (Range) | 18.45 ± 11.04 (4 – 100) |

## *Results*

In total, 80 subjects were included in the analysis, which a mean age was 57.98 ± 8.85 years (range 39-76), a mean BMI of 29.98 ± 3.82, and 40 (06.47%) patients were male (Table 1).

There is a significant inverse relationship between SNAR and the duration of diabetes, and this correlation is high ($r = - 0.7$, $p<0.001$). There is also a significant inverse relationship between SRAR and the duration of diabetes, and this correlation is high ($r = - 0.702$, $p<0.001$) (Table 2).

Comparing the correlation between the duration of diabetes and the SNAR with the correlation between the duration of diabetes and the SRAR

***Table 2.***

Evaluation of the relationship between the sensory domain of the sural nerve and the sensory domain of the radial nerve to the age, duration of diabetes, and body mass index (BMI).

| Variables | SNAR group | | SRAR group | |
|---|---|---|---|---|
| | r | P-value* | r | P-value* |
| Age | - 0.76 | < 0.001 | - 0.762 | < 0.001 |
| Duration of DM | - 0.70 | < 0.001 | - 0.702 | < 0.001 |
| BMI | 0.051 | 0.64 | 0.045 | 0.683 |

***Note:*** ** Spearman Correlation test*

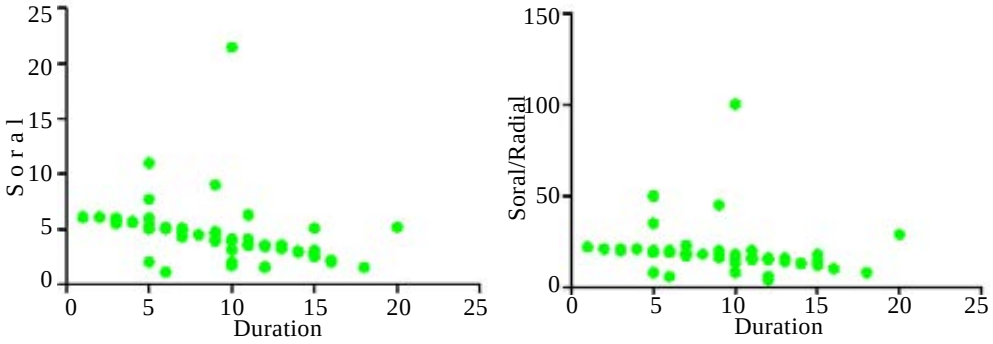


***FIGURE 1.*** *Distribution diagrams between the sensory domain of the sural nerve and the sensory domain of the sural nerve to the radial with the duration of diabetes.*

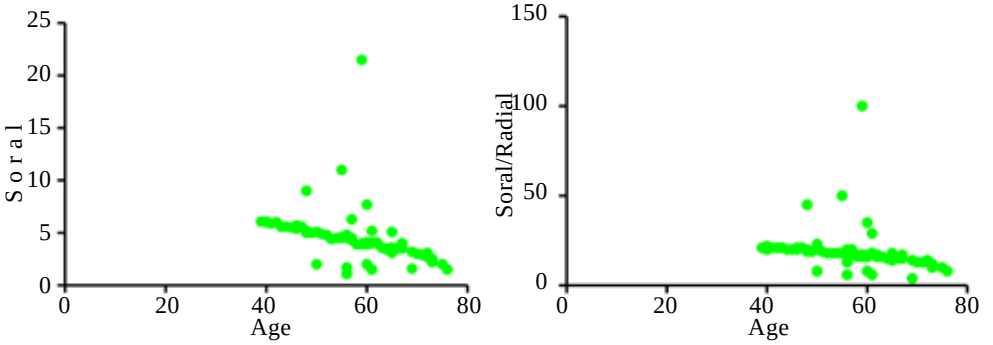


***FIGURE 2.*** *Distribution diagrams between the sensory domain of the sural nerve and the sensory domain of the sural nerve to the radial with the age of patients with diabetes.*

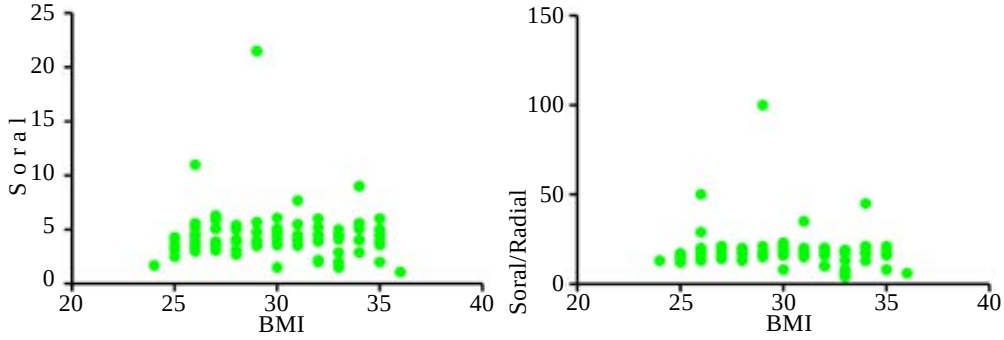


***FIGURE 3.*** *Distribution diagrams between the sensory amplitude of the sural nerve and the sensory amplitude of the sural to radial with the BMI of patients with diabetes*

showed was no statistically significant difference between these two correlations (p=0.89) (Fig. 1). There is a significant inverse relationship between the SNAR and the age of patients with diabetes, and this correlation is high (r = - 0.76, p<0.001). There is a significant inverse relationship between SRAR and the age of patients with diabetes, and this correlation is high (r = - 0.762, p<0.001) (Table 2). Also, the comparison between the correlation between age and SNAR with the correlation between age and SRAR to the radial showed was no statistically significant difference between these two correlations (p=0.88) (Fig. 2).

There is a non-significant direct correlation between the SNAR and SRAR with the BMI of patients with diabetes, and this correlation is negligible (p>0.05) (Table 2 and Fig. 3). The results showed no statistically significant difference between the sensory amplitude of the sural nerve in men and women (p=0.546). Also, there is no statistically significant difference between SRAR of men and women (p=0.695) (Table 2). There is a non-significant direct correlation between the SNAR and SRAR, to diagnose patients with and without neuropathy (p=0.625) (Table 3).

### *DISCUSSION*

Previously, the clinical and neurophysiologic manifestations of severe sural neuropathy were observed in a group of diabetic individuals with severe systemic problems [*Nattero-Chávez L et al., 2022; Papanas N et al., 2019*], In addition, distal symmetrical polyneuropathy is the most common form of diabetic neuropathy [*Kakrani A et al., 2014*]. On the other hand, the automated nerve conduction study of the sural nerve using electro-

***Table 3.***

The frequency and percentage of diabetic patients with and without neuropathy based on the SNAR and the SRAR.

| Variable | | SNAR group n (%) | SRAR group n (%) | P-Value* |
|---|---|---|---|---|
| **Neuropathy** | Yes | 76 (89.41) | 78 (91.76) | 0.625 |
| | No | 9 (10.59) | 7 (8.24) | |

***Note:*** ** McNemar's test*

diagnosis equipment is compassionate and specific for diagnosing diabetic peripheral neuropathy in type 2 diabetes mellitus [*Chatzikosma G et al., 2016*], In this case, a study provided the same results and showed that sural had a high diagnostic value for routine peripheral neuropathy screening [*Vrancken A et al., 2008*]. Moreover, SRAR has high sensitivity and moderate specificity for neuropathy diagnosis. In addition, it is a strong and independent factor for diagnosis [*Papanas N et al., 2007; 2020*].

In this cross-sectional study, no significant difference was observed between the two electrophysiological methods from the sensitivity viewpoint. Both approaches were equally effective in diagnosing patients with diabetic neuropathy. In a study accomplished by Barnett C. and colleagues (2012), the authors did not find an advantage for SRAR over SNAP alone in diagnosing sensory poly neuropathy for type 2 diabetes. However, Turgut N. and co-authors (2006) demonstrated that SRAR was a more sensitive method than SNAP alone for measuring mild axonal neuropathy.

The present study evaluated and compared the affectability of the two methods based on age, sex, BMI, and duration of diabetes. In this case, both approaches had the same affectability on the duration of diabetes. Indeed, the longer duration of diabetes identically lowered SRAR and SNAP. Some studies showed that variables such as age and BMI had an adverse effect on SNAP, while SRAR was negligibly affected by these variables [*Koçer A et al., 2007*], It was found that sural nerve amplitude was inversely related to diabetes duration [*Hamasaki H, Hamasaki Y, 2017*]. Although SRAR was not affected by the variables such as sex, weight, and height, it was impacted by age. However, these variables strongly influenced SNAP, which is more sensitive to early detection of sensory polyneuropathy. In addition, SRAR only enhanced the specificity of the study and had no other value in the diagnosis of distal sensory polyneuropathy [*Overbeek B et al., 2005*]. On the other hand, these studies indicated that SRAR was a sensitive, specific, age-specific, and electrodiagnostic test for measuring mild axonal polyneuropathy [*Sumner C et al., 2003; Sasak H et al., 2020*].

The type of diabetes affects the sensitivity of the test. In type 1 diabetes, the sensory amplitude of the sural nerve to the radial ratio is related to the course of the disease. Also, it is the first parameter that decreases significantly. In both types of diabetes, SRAR is the first test for diagnosing diabetic polyneuropathy [*Pastore C et al., 1999; Dunnigan S et al., 2013*]. It can be attributed to the lack of proper control of diabetes, the passage of time, and the exacerbation of neuropathy. In addition, these methods have the same affectability on the patient's age. In other words, the older the patient, the lower the SNAP and SRAR by the identical amounts. To justify this issue, we can point to the affectability of nerve amplitude by aging as it usually decreases with age. However, the methods had the same affectability on patients' BMI. Indeed, the patients' BMI increment was associated with a slight reduction in both SNAP and SRAR.

**Limitations**

The study limitations include limited sample size, a lack of a broad population, and the absence of a control group.

## *Conclusion*

The findings demonstrated that SRAR was a promising method for detecting neuropathy in patients with type 2 diabetes. SRAR and SNAR had a significant inversion relationship with age and duration of diabetes for detecting diabetic neuropathy in type 2 diabetes patients.

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## CONTENTS

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**Address for correspondence:**

Yerevan State Medical University
2 Koryun Street, Yerevan 0025,
Republic of Armenia

**Phones:**

(+37410) 582532 YSMU
(+37493 588697 Editor-in-Chief
**Fax:** (+37410) 582532
**E-mail:** namj.ysmu@gmail.com, ysmiu@mail.ru
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