Is There A Relation Between Peripheral Nerves Conduction Study and Cardiovascular Assessment in Men with Type 2 Diabetes Mellitus? (A Cross-Sectional Study)

Eman Abd El Aziz Galbat¹, Samah Samy Youssef², Mai Mohamed Abdelraof Salman², Asmaa Abdel Raheem Abdel Latif³, Doaa Salah Elgendy⁴, Maha Mohamed Abdelraof Salman*¹

Departments of ¹Physical Medicine, Rheumatology, and Rehabilitation, ²Cardiology, ³Public Health and Community Medicine (Industrial Medicine and Occupational Health Specialty) and ⁴Internal Medicine (Endocrinology Unit), Faculty of Medicine, Menofia University, Menofia Governorate, Egypt

*Corresponding author: Maha Mohamed Abdelraof Salman, Mobile: (+20) 01096897968, E-Mail: mhasalan200@gmail.com

ABSTRACT

Background: Heart disease is thought to be dangerously increased by type two diabetes mellitus. Type two diabetic individuals have 2-3 times higher incidence of cardiovascular diseases. There are a few research using nerve conduction investigations to demonstrate the relationship between diabetic peripheral neuropathy and cardiovascular problems. The existence of diabetic neuropathy may be associated to atherosclerosis.

Objective: The target of this study is to analyze the mechanism between nerve conduction study (NCS) and cardiovascular evaluation in type two diabetes mellitus affected males.

Patients and Methods: This cross-sectional study included 105 males type-2 diabetes mellitus cohort with body mass index between 18.5-25, normal blood pressure and normal lipid profile. Nerve conduction studies of (median, tibial and sural nerves) were performed and cardiovascular detection of left ventricular function using 2D-speckle tracking echocardiography and peripheral vascular resistance using ankle-brachial index were assessed.

Results: In this study poor glycemic control was correlated with the severity of diabetic peripheral neuropathy (p < 0.05). Nerve conduction studies showed highly significant negative correlation between sensory, motor latency, F latency and global strain (p < 0.001), while highly significant positive correlation with motor and sensory conduction velocity and amplitude was found (p < 0.001). Regarding ankle-brachial index, there was highly significant positive correlation with global strain on both sides (p < 0.001). There was an association between diabetic peripheral neuropathy and altered ankle-brachial index scores as there was significant correlation with the neuropathic parameters of the studied nerves (p < 0.05).

Conclusions: According to nerve conduction studies, arterial stiffness and cardiac parameters deteriorate along with diabetic neuropathy. Males with type-2 diabetes mellitus who undergo nerve conduction studies may benefit from early neuropathy identification as well as preclinical left ventricular dysfunction prediction.

Keywords: Type 2 Diabetes Mellitus, Nerve Conduction Study, Diabetic Peripheral Neuropathy, 2D Speckle Tracking Echo, Ankle Brachial Index.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is regarded as a potentially harmful cardiovascular (CVD) risk factor. Compared to non-diabetics of the same age, type two diabetic individuals have 2-3 times higher incidence of CVD. Extensive glycemic control, however, can't decrease the hazard of heart complications and death rate in T2DM cohort, according to prior research. Clarifying the factors linked to CVD occurrence is therefore urgently needed [¹].

As with retinopathy and nephropathy, diabetic peripheral neuropathy (DPN) is a microvascular consequence of diabetes. The most frequent factor in morbidity and disability among diabetic individuals has been identified as DPN [²].

DPN is also said to have an impact on mortality and quality of life. Previous research indicated a connection between cardiovascular events and diabetic microvascular problems. Retinopathy, for instance, is linked to ischemic stroke and coronary heart disease. Additionally, micro-albuminuria is connected to significant CV events [³].

In addition, a prior extensive prospective investigation has demonstrated that subjects with diabetic neuropathy of the cardiac autonomic nerves had a twofold higher mortality rate than those without it [⁴].

Microvascular problems in diabetics increase the hazard of CVS events and death rate. Several studies demonstrated that the existence of diabetic neuropathy might be connected to sclerosis of blood vessels [⁴]. Investigation of the nerve conduction (NC) is a good quantitative approach for determining the severity of DPN and is typically used to identify nerve function in clinical situations. However, the correlation between DPN and cardiovascular problems has only been studied in a small number of studies employing nerve conduction (NC) testing [⁵].

AIM OF THE WORK

In males with T2DM, left ventricular function using two D speckle tracking echo (STE) and peripheral vascular resistance measured by ankle brachial index, were assessed in relation to peripheral nerves (median, tibial and sural) conduction studies; so as to detect the
the average was measured. The ankle brachial index (ABI) was calculated. A resting ABI score of less than or equal 0.9 defines the existence of peripheral arterial disease, with a sensitivity of approximately 95% and specificity about 100% in identifying hemodynamically significant arterial stenosis \(^{10}\).

**Nerve Conduction Study (NCS):**

NCS was done as motor study of the median and tibial and sensory study for the median and sural nerves. The parameters evaluated included; distal motor latencies (DML), amplitude measured from baseline to negative peak, mean F-wave latency, sensory peak latencies (SL) measured to negative peak, and amplitude measured from negative to positive peak and conduction velocity for all nerves. After adjusting the patient's age and size, if the reading was out of the normal range, the reading was flagged as abnormal. The usual limit was 97.5 latency parameter percentile and 2.5 percentile set to amplitude. Borders were flagged to (90-97.5) percentiles for delays and the (2.5-10) percentiles for amplitudes \(^{11}\).

**Ethical consent:**

The patients were informed in detail about the purpose of the study, and written consent was obtained for their participation in the study. Ethical approval was obtained from the Ethical Committee at Faculty of Medicine, Menoufia University with IRB (Institutional Review Board approval number and date 62021PMR3). This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Statistical analysis**

Results were collected, tabulated and statistically analyzed by an IBM compatible personal computer with SPSS statistical package version 20. a) Descriptive statistics: mean, standard deviation (SD) and range were calculated. b) Analytic statistics: Pearson correlation coefficient test (r-test) was used to study the correlation between two quantitative variables while Spearman correlation coefficient test was used to study the correlation between nonparametric quantitative variables. P value < 0.05 was considered significant.

**RESULTS**

The study included 105 male patients with type 2 DM. The motor median study revealed delayed mean motor latency with normal amplitude and velocity, while the sensory study showed neuropathic parameters. The tibial and sural studies showed normal mean values. The mean ankle-brachial index (ABI) indicates the presence of peripheral arterial resistance (< 0.9), while the left ventricular global strain was borderline (Table 1).
Poor diabetic control was correlated with the severity of the PN in the study group. Patients with higher HbA1c had significantly abnormal sensory values in the median and sural nerves, and abnormal motor latency and velocity in median and tibial nerves (Table 2).

Table (2): Correlation between HbA1c and other studied parameters

<table>
<thead>
<tr>
<th>Studied parameters</th>
<th>HbA1c</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td></td>
</tr>
<tr>
<td><strong>Median nerve (motor):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency</td>
<td>0.21</td>
<td>0.032*</td>
</tr>
<tr>
<td>Amplitude</td>
<td>-0.12</td>
<td>0.207</td>
</tr>
<tr>
<td>Conduction velocity</td>
<td>-0.26</td>
<td>0.022*</td>
</tr>
<tr>
<td>F latency</td>
<td>0.17</td>
<td>0.091</td>
</tr>
<tr>
<td><strong>Median nerve (sensory):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak latency</td>
<td>0.36</td>
<td>0.003*</td>
</tr>
<tr>
<td>Amplitude</td>
<td>-0.28</td>
<td>0.007*</td>
</tr>
<tr>
<td>Velocity</td>
<td>-0.24</td>
<td>0.016*</td>
</tr>
<tr>
<td><strong>Sural nerve (sensory):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak latency</td>
<td>0.18</td>
<td>0.051</td>
</tr>
<tr>
<td>Amplitude</td>
<td>-0.31</td>
<td>0.002*</td>
</tr>
<tr>
<td>Velocity</td>
<td>-0.22</td>
<td>0.025*</td>
</tr>
<tr>
<td><strong>Tibial nerve (motor):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency</td>
<td>0.22</td>
<td>0.027*</td>
</tr>
<tr>
<td>Amplitude</td>
<td>-0.14</td>
<td>0.151</td>
</tr>
<tr>
<td>Conduction velocity</td>
<td>-0.53</td>
<td>0.005*</td>
</tr>
<tr>
<td>F latency</td>
<td>0.40</td>
<td>0.009*</td>
</tr>
<tr>
<td><strong>Global strain</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-0.17</td>
<td>0.055</td>
</tr>
<tr>
<td><strong>Right ABI</strong></td>
<td>-0.47</td>
<td>0.004*</td>
</tr>
<tr>
<td><strong>Left ABI</strong></td>
<td>-0.29</td>
<td>0.015*</td>
</tr>
</tbody>
</table>

ABI: Ankle-Brachial Index   HbA1c: Hemoglobin A1c
*: Significant

Global strain had statistically significant negative correlation with motor, sensory and F latencies in median, tibial and sural nerves. On the other hand, it had a highly significant positive correlation with the motor and sensory amplitude in both median and tibial nerves. Also, there was highly significant positive correlation between the global strain and ankle brachial index on both sides (Table 3).
**Table (3): Correlation between cardiac parameters and nerve conduction parameters**

<table>
<thead>
<tr>
<th>Studied parameters</th>
<th>Global strain</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>-0.14</td>
<td>0.235</td>
</tr>
</tbody>
</table>

**Median nerve (motor):**
- Latency: -0.24, 0.015*
- Amplitude: 0.35, 0.003*
- Conduction velocity: 0.55, <0.001**
- F latency: -0.61, <0.001**

**Median nerve (sensory):**
- Peak latency: -0.44, <0.001**
- Amplitude: 0.51, <0.001**
- Velocity: 0.28, 0.025*

**Sural nerve (sensory):**
- Peak latency: -0.23, 0.019*
- Amplitude: 0.19, 0.045*
- Velocity: 0.31, 0.002*

**Tibial nerve (motor):**
- Latency: -0.28, 0.004*
- Amplitude: 0.47, <0.001**
- Conduction velocity: 0.73, <0.001**
- F latency: -0.53, <0.001**

**Right ABI**
- 0.49, <0.001**

**Left ABI**
- 0.69, <0.001**

ABI: ankle-brachial index  
*: Significant, **: Highly significant

An association between diabetic neuropathy and altered ABI scores was proved by the significant correlation with the neuropathic parameters of the nerves. There was highly significant positive correlation of ABI with both motor and sensory amplitude and velocity of both median and tibial nerves. On the other hand, there was a significant negative correlation between ABI and F wave latency for both median and tibial nerves (Table 4).

**Table (4): Correlation between ankle brachial index and nerve conduction parameters**

<table>
<thead>
<tr>
<th>Studied parameters</th>
<th>Right ABI</th>
<th>Left ABI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P-value</td>
</tr>
<tr>
<td>Age (years)</td>
<td>-0.17</td>
<td>0.071</td>
</tr>
</tbody>
</table>

**Median nerve (motor):**
- Latency: -0.09, 0.451
- Amplitude: 0.55, <0.001**
- Conduction velocity: 0.41, <0.001**
- F latency: -0.34, <0.001**

**Median nerve (sensory):**
- Peak latency: -0.08, 0.391
- Amplitude: 0.44, <0.001**
- Velocity: 0.48, <0.001**

**Sural nerve (sensory):**
- Peak latency: -0.26, 0.021*
- Amplitude: 0.52, <0.001**
- Velocity: 0.56, <0.001**

**Tibial nerve (motor):**
- Latency: -0.44, 0.002*
- Amplitude: 0.48, <0.001**
- Conduction velocity: 0.36, <0.001**
- F latency: -0.31, 0.007*

Right ABI with right side parameters and left ABI with left side, ABI: ankle-brachial index  
*: Significant, **: Highly significant

**DISCUSSION**
In this study, bad glycemic control correlated with the severity of PN in cases with type two DM. This matches with the results of Lai et al. \cite{12} as they concluded that elevated HbA1c levels were related to lower values for amplitude and conduction of the tested nerve. Similarly, one study found that diabetic patients with HbA1c levels six to seven percent had significantly reduced median and ulnar nerve conduction velocity compared to diabetic patients with HbA1c five to six percent \cite{13}. In another study, HbA1c levels in T2DM patients aged 40-70 years showed an adverse relation with nerve conduction study (NCV) in the ulnar and tibial nerve \cite{14}.

In this study, HbA1c was significantly negatively correlated with motor velocity, sensory amplitude and NCV, similar to many studies conducted in India, and the United Kingdom \cite{15,16}. Peterson et al. \cite{17} showed a decrease in amplitude of sural nerve, with elevated HbA1c measurements, and axonal degeneration was earlier and more pronounced than demyelination due to the effects of hyperglycemia. In contrast to our results; a cross-sectional study by Hamid et al. \cite{18} revealed a significant negative relation between duration and median nerve amplitude, but not with HbA1C. The deceleration of NCV is due to continued degeneration of the myelin sheath, and the amplitude decreases with increasing HbA1c measurements, leading to the development and progression of nerves disorders. In addition, for every one percent increase in HbA1c, the incidence of diabetic neuropathy increases by approximately ten to fifteen percent \cite{19}.

Another observational cohort study found that the density of myelin sheath in the sural nerve biopsy was significantly associated with the control of DM \cite{20}. HbA1c level was a quantitative indicator of the severity of multiple neuropathy \cite{21}.

Low ABI and elevated levels of HbA1c were both risk factors for heart diseases. Our results showed a negative correlation between ABI and HbA1c. Elmassry et al. \cite{22} and Liu et al. \cite{23}, stated that HbA1c independently and linearly correlated with the left and right ABI. Keeping HbA1c under control resulted in reduction of the risk of cardiovascular disease in T2DM \cite{24}. However, a Chinese study reported that ABI isn't a risk factor for heart diseases in type 2 DM patients in China, especially older females \cite{25}.

GLS abnormality is associated with CV risk in diabetic patients who had no history of CV problems. GLS more than (−17.9) represents an excellent negative predictor for CV diseases. Addressing these parameters by echocardiography help improving risk stratification in patients with T2DM without cardiovascular complications \cite{26}.

In this study, GLS showed a significant inverse correlation with HbA1c. This is consistent with a study by Silveri et al. \cite{27} in patients with type 2 DM free of CVD, multivariate regression of LV GLS containing only HbA1c, age, gender, and BMI retained statistical significance. Thus, patients with type 2 DM have reduced longitudinal left ventricular strain independent of microvascular complications and appear to be accompanied with glucose dysregulation and ANS dysfunction.

Another study found a significant correlation between HbA1c and GLS. The analysis found no significant correlation between BMI and GLS, however, high HbA1C levels correlated with worsening overall left ventricular GLS as a mark of hidden heart muscle dysfunction \cite{28}.

In the current study, for motor and sensory studies, GLS had statistically significant negative correlation with distal motor, and F latencies, and positive correlation with motor velocity and amplitude. There was a significant negative correlation between mean sensory peak latency and a significant positive correlation between sensory conduction rates and amplitudes. A highly significant positive correlation was found between GLS and ABI on both sides.

Mochizuki et al. \cite{29} provided the first evidence that diabetic neuropathy was associated with impaired left ventricular systolic function in asymptomatic patients with preserved ejection fraction. Furthermore, only the F minimal latency was independently associated with subclinical left ventricular systolic dysfunction.

Sacre et al. \cite{30} had a proof of asymptomatic abnormalities in systole and diastole of LV in cases with type two diabetes with cardiac neuropathy. In their study population, 16 patients (14%) suffered from cardiac neuropathy, and the Doppler-peak systolic and early diastolic rates of stained tissue were faster than those without cardiac autonomic neuropathy. This finding indicates that patients with cardiac autonomic neuropathy, despite the preservation of LV ejection fraction, have impaired longitudinal function of LV in systole and diastole, it was significantly lower.

Many studies have reported that F-wave latency as the excellent predictor of DN, moreover; F-wave latency shows correlation with GLS, suggesting the first proof to confirm the existence of asymptomatic abnormality in the muscular function of left ventricle \cite{30}. Research by Tanaka et al. \cite{31} in T2DM atherosclerosis revealed the presence of DPN after adjusting the common risk factors for atherosclerosis such as age, diabetic duration, BMI, BP, BLG, serum lipids, and proteinuria. It has been shown to be related to these parameters and cardiovascular events.

Yokoyama et al. \cite{32} demonstrated that brachial pulse pressure was significantly associated with the presence of diabetic neuropathy. In addition, DPN is accompanied with the heart abnormality risk in type two diabetes. They also concluded that DPN was accompanied with arteriosclerosis in T2DM cases and NCV is a clinical prediction of cardiovascular disease.
independent of conventional risk factors. These results showed that the degree of DPN may be accompanied by heart vessels complications.

In this study, there was a positive correlation between ABI and age in patients with type two diabetes, but it was not significant. Chevtchouk et al. [33] proposed a correlation of ABI score and advancing age. They also supported the association between diabetic neuropathy and altered ABI scores, as evidenced in this study by the significant correlation with the neuropathy parameters of the median, tibial, and sural nerve conduction tests. The correlation was very significantly positive for both the motor unit action potentials amplitude and conduction velocity of both the median and tibial nerves, and the sensory amplitude and conduction velocity of both the median and sural nerves. There was a significant negative correlation between ABI and F-wave latency in both the median and tibial nerves.

Lee and Hsieh [34] also found a significant relationship between DPN severity (based on NCS results) and PAD. This was indicated by the ABI score being < 0.9. The correlation was mainly found in the lower extremity NCS; the motor action potential amplitude and velocity of both tibial and sensory nerves / sural nerve amplitude and NCV. Meanwhile, Nguyen et al. [35] found that there was no correlation between ABI scores and DPN symptoms, signs, or NCS abnormalities in seventy-three patients with type two diabetes.

**STUDY LIMITATIONS**

This study included small number of cases, so a big-scale case study in the future is needed to validate the results. In addition, the absence of controls was also a limitation.

**CONCLUSIONS**

Diabetic neuropathy estimated by NCS is linearly accompanied with the abnormality of arterial elasticity and cardiac parameters in type 2 diabetic patients independently of various diabetic and other factors that lead to vessels stiffness. Performing NCS as a routine study in males with T2DM may help in early identification of neuropathy and subtle LV abnormality in patients without symptoms.

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**Conflict of interest:** Nil.

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