The Egyptian Journal of Hospital Medicine (October 2022) Vol. 89 (2), Page 7302- 7308

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 Galbat[1], Samah Samy Youssef[1], Mai Mohamed Abdelraof Salman[2], Asmaa Abdel Raheem Abdel Latif[3], Doaa Salah Elgendy[4], Maha Mohamed Abdelraof Salman*[1]

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

***Corresponding author:** Maha Mohamed Abdelraof Salman, **Mobile:** (+20) 01096897968, **E-Mail:** mhasalman200@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

Received: 15/7/2022
Accepted: 18/9/2022

relationship between NC and parameters of the cardiovascular system.

PATIENTS AND METHODS

In this cross-sectional investigation, 105 males with T2DM were enrolled from the rheumatology and rehabilitation outpatient clinic at Menoufia University Hospital. Inclusion criteria included: age > 18 years, BMI between 18.5-25, normal lipid profile, normal blood pressure and excluding any other potential neuropathies.

Length (centimeter) was measured with a studio meter [6], which is the upright distance from the sole of the foot to the crown, and body weight (kilogram) was measured and recorded, while light clothes were worn by the patient; using a medical electronic scale. The BMI was obtained by dividing the body weight in kilograms by the square of the body length in meters, and its unit is kg/m^2. In this study, the acceptable BMI range as normal body weight was (18.5 -25) [7].

After five-minutes of resting in the supine posture, blood pressure (millimeter mercury) was assessed using a mercurial sphygmomanometer. Blood was taken after the subjects had fasted the previous night. Using high performance liquid chromatography, HbA1c was calculated. Standard enzymatic techniques were used to measure serum creatinine, fasting plasma glucose (FPG), fasting C-peptide, total cholesterol (TC), triglycerides (TG), high density lipoprotein-cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C). All were tested to rule out patients with aberrant lipid profiles or blood pressure. Also, albuminuria was evaluated using storage urine collected over a twenty-four-hour period.

Detection of left ventricular function and peripheral vascular resistance (PVR):

***Assessment of global strain (GLS)**: Using a single specialized piece of software, GLS was evaluated using two D STE from the 3 common apical viewpoints (EchoPAC version 113; GE Vingmed). For each of the three apical views, a region of interest was quickly delineated on the endocardium at end-systole using a point-and-click method [8].

***Ankle brachial index [9].**

After the person rested in the supine position for five minutes systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the brachial arteries of both arms were recorded using a mercury sphygmomanometer. The best systolic measurements were measured on both arms as the first persistent noise audible pressure. 2 or more measurements were taken on the same arm and the average was measured as the SBP of the arm. In all patients, ankle pressure was measured on 2 ankles by a Doppler equipped with a gold standard 8MHz probe. The leg with low SBP was used as the reference leg. 2 or more readings were made and 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).

Table (1): Description Statistics

	Minimum	Maximum	Mean	Standard Deviation
Median nerve (motor): - Latency	3.2	6.7	4.74	1.11
- Amplitude	2.5	12.3	6.96	1.35
- Velocity	40	68.75	53.41	6.34
Median F Latency.	24.00	37.24	30.11	2.78
Median nerve (sensory): - Peak latency	2.8	5.21	3.62	2.79
- Amplitude	3.00	33.75	14.92	3.59
- Velocity	35.00	60.45	39.80	9.42
Tibial nerve (motor): - Latency	3.08	5.42	4.09	0.66
- Amplitude	2.68	8.34	6.29	1.32
- Velocity	27.05	55.00	45.83	9.70
Tibial F latency	35.65	59.00	52.58	2.19
Sural nerve (sensory): -Peak latency	3.8	5.48	4.19	1.03
-Amplitude	4.00	20.90	8.63	2.03
-Velocity	33.00	60.05	43.37	9.83
Ankle-Brachial Index (ABI)	0.70	1.00	0.83	0.08
Global strain	13	20	-16.83	2.16

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

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

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

Studied parameters	Global strain	
	r	P-value
Age (years)	-0.14	0.235
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

Studied parameters	Right ABI		Left ABI	
	r	P-value	r	P-value
Age (years)	-0.17	0.071	-0.09	0.352
Median nerve (motor):				
Latency	-0.09	0.451	-0.12	0.227
Amplitude	0.55	**<0.001****	0.55	**<0.001****
Conduction velocity	0.41	**<0.001****	0.56	**<0.001****
F latency	-0.34	**<0.001****	-0.19	**0.028***
Median nerve (sensory):				
Peak latency	-0.08	0.391	-0.25	**0.011***
Amplitude	0.44	**<0.001****	0.42	**<0.001****
Velocity	0.48	**<0.001****	0.41	**<0.001****
Sural nerve (sensory):				
Peak latency	-0.26	**0.021***	-0.41	**<0.001****
Amplitude	0.52	**<0.001****	0.25	**0.010***
Velocity	0.56	**<0.001****	0.50	**<0.001****
Tibial nerve (motor):				
Latency	-0.44	**0.002***	-0.23	**0.019***
Amplitude	0.48	**<0.001****	0.55	**<0.001****
Conduction velocity	0.36	**<0.001****	0.35	**0.003***
F latency	-0.31	**0.007***	-0.38	**0.002***

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.*** [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 [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 [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 [15, 16]. **Peterson *et al.*** [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.*** [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 [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 [20]. HbA1c level was a quantitative indicator of the severity of multiple neuropathy [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.*** [22] **and Liu *et al.*** [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 [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[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 [26].

In this study, GLS showed a significant inverse correlation with HbA1c. This is consistent with a study by **Silverii *et al.*** [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 [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.* [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.* [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 [30]. Research by **Tanaka *et al.*** [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.* [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, **Nguyenf *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.

Financial support and sponsorship: Nil.
Conflict of interest: Nil.

REFERENCES

1. **Ishihara M, Kojima S, Sakamoto T *et al.* (2009):** Comparison of blood glucose values on admission for acute myocardial infarction in patients with versus without diabetes mellitus. Am J Cardiol., 104: 769–774.
2. **Ward R, Caserotti P, Cauley J *et al.* (2016):** Mobility-related consequences of reduced lower-extremity peripheral nerve function with age: a systematic review. Aging Dis., 7: 466–478.
3. **Cheung N, Wang J, Klein R *et al.* (2007):** Diabetic retinopathy and the risk of coronary heart disease: the Atherosclerosis Risk in Communities Study. Diabetes Care, 30: 1742–1746.
4. **Brownrigg R, de Lusignan S, McGovern A *et al.* (2014):** Peripheral neuropathy and the risk of cardiovascular events in type 2 diabetes mellitus. Heart, 100: 1837–1843.
5. **Ando A, Miyamoto M, Kotani K *et al.* (2017):** Cardio-ankle vascular index and indices of diabetic polyneuropathy in patients with type 2 diabetes. J Diabetes Res., 17: 2810914. doi: 10.1155/2017/2810914.
6. **Stem M, Hussain M, Lentz S *et al.* (2014):** Differential reduction in corneal nerve fiber length in patients with type 1 or type 2 diabetes mellitus. J Diabetes Complicat., 28:658–661.
7. **World Health Organization (2019):** Body Mass Index (BMI). https://www.who.int/data/gho/ data/themes/ topics/topic-details/GHO/body-mass-index
8. **Lang R, Badano L, Mor-Avi V *et al.* (2015):** Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr., 28(1):1–39.
9. **American Diabetes Association (2003):** Peripheral arterial disease in people with diabetes. Diabetes Care, 26(12):3333-41.
10. **Rooke T, Hirsch A, Misra S *et al.* (2011):** 2011 ACCF/AHA focused update of the guideline for the management of patients with peripheral artery disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology, 58(19):2020-45.
11. **England J, Gronseth G, Franklin G *et al.* (2005):** Distal symmetric polyneuropathy: a definition for clinical research: report of the American Academy of Neurology, the American Association of Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. Neurology, 64(2):199–207.
12. **Lai Y, Chiu W, Huang C *et al.* (2019):** HbA1C variability is strongly associated with the severity of peripheral neuropathy in patients with type 2 diabetes. Front. Neurosci., 13: 90-94.
13. **Farheen A, Malipatil S, Gousuddin A (2015):** Nerve conduction in type 2 diabetics and its correlation with glycosylated haemoglobin. Journal of Evolution of Medical and Dental Sciences, 4: 1023-34.
14. **Saeed S, Akram M, Mahmood Q (2009):** Glycemic control as a predictor of diabetic neuropathy. Pakistan Journal of Medical and Health Sciences, 3(2): 153-7.
15. **Masood A, Rizvi S, Siddiqi S *et al.* (2019):** A study on effects of HbA1c levels on nerve conduction velocity in type 2 diabetes mellitus patients. Int J Cur Res Rev., 11(03):6–8.
16. **Sunandini R, Somani S (2016):** Median nerve conduction velocity as a tool to detect subclinical neuropathy in type II diabetes mellitus. Int J Physiol., 4(1):103–9.
17. **Peterson M, Pingel R, Lagali N *et al.* (2017):** Association between HbA1c and peripheral neuropathy

in a 10-year follow-up study of people with normal glucose tolerance, impaired glucose tolerance and type 2 diabetes. Diabetic Med., 34(12):1756–64.

18. **Hamid W, Ahmed H, Osman M *et al.* (2021):** Nerve conduction and its correlations with duration of diabetes mellitus and glycosylated haemoglobin in type 2 diabetes mellitus (T2DM). Journal of Endocrinology, Metabolism and Diabetes of South Africa, 26:46-51.
19. **Bansal V, Kalita J, Misra U (2006):** Diabetic neuropathy. Postgrad Med J., 82:95-100.
20. **Perkins B, Greene D, Bril V (2001):** Glycemic control is related to the morphological severity of diabetic sensorimotor polyneuropathy. Diabetes Care, 24: 748–752.
21. **Lee W, Jang S, Lee S *et al.* (2016):** Correlation between the severity of diabetic peripheral polyneuropathy and glycosylated hemoglobin levels: A quantitative study. Ann Rehabil Med., 40(2):263-70.
22. **Elmassry M, Abdelmalek J, Prieto S *et al.* (2021):** Impact of type 2 diabetes and obesity on the left ventricular global longitudinal strain: a retrospective review. J Chest, 160(4): A1498. DOI:10.1016/j.chest.2021.07.1370.
23. **Liu H, Liu J, Zhao H *et al.* (2019):** Relationship between glycated hemoglobin and low Ankle-Brachial Index: a cross-sectional observational study from the Beijing Vascular Disease Evaluation Study (BEST Study). Int Angiol., 38(6): 502-507.
24. **Sun K, Liu Z, Cao Y *et al.* (2015):** Relationship between brachial-ankle pulse wave velocity and glycemic control of type 2 diabetes mellitus patients in Beijing community population. Beijing Da Xue Xue Bao Yi Xue Ban., 47(3):431-6.
25. **Xu L, He R, Hua X *et al.* (2019):** The value of ankle-branchial index screening for cardiovascular disease in type 2 diabetes. Diabetes Metab Res Rev., 35(1): e3076. doi: 10.1002/dmrr.3076.
26. **Liu J, Chen Y, Yuen M *et al.* (2016):** Incremental prognostic value of global longitudinal strain in patients with type 2 diabetes mellitus. Cardiovasc Diabetol., 15: 22. doi: 10.1186/s12933-016-0333-5.
27. **Silverii G, Toncelli L, Casatori L *et al.* (2022):** Assessment of left ventricular global longitudinal strain in patients with type 2 diabetes: Relationship with microvascular damage and glycemic control. Nutr Metab Cardiovasc Dis., 32(4):994-1000.
28. **Leung M, Wong V, Hudson M *et al.* (2016):** Impact of improved glycemic control on cardiac function in type 2 diabetes mellitus. Circ Cardiovasc Imaging, 9(3):e003643. doi: 10.1161/CIRCIMAGING.115.003643.
29. **Mochizuki Y, Tanaka H, Matsumoto K *et al.* (2015):** Association of peripheral nerve conduction in diabetic neuropathy with subclinical left ventricular systolic dysfunction. Cardiovasc Diabetol., 14:47. doi: 10.1186/s12933-015-0213-4
30. **Sacre J, Franjic B, Jellis C *et al.* (2010):** Association of cardiac autonomic neuropathy with subclinical myocardial dysfunction in type 2 diabetes. J Am Coll Cardiol Img., 3(12):1207–15.
31. **Tanaka S, Kanazawa I, Sugimoto T (2018):** Nerve conduction velocity is negatively associated with intima-media thickness and brachial-ankle pulse wave velocity in men with type 2 diabetes mellitus. PLoS One, 13(12): e0209503. https://doi.org/10.1371/journal.pone.0209503
32. **Yokoyama H, Yokota Y, Tada J *et al.* (2007):** Diabetic neuropathy is closely associated with arterial stiffening and thickness in type 2 diabetes. Diabet Med., 24: 1329–1335.
33. **Chevtchouk L, da Silva M, Nascimento O (2017):** Ankle-brachial index and diabetic neuropathy study of 225 patients. Arq Neuropsiquiatr., 75(8):533-538
34. **Lee Y, Hsieh L (2017):** Relationship between peripheral vessels and electrophysiological examination in patients with diabetic peripheral neuropathy. Cheng Ching Medical Journal, 13(2):9–14.
35. **Nguyenf V, Phan H, Hoang T *et al.* (2021):** Correlation between the ankle–brachial index and microalbuminuria with certain risk factors in type 2 diabetes patients. Cardiovasc Endocrinol Metab., 10(4): 210–214.