Original Article
http://mjiri.iums.ac.ir
Medical Journal of the Islamic Republic of Iran (MJIRI)

Med J Islam Repub Iran. 2024 (7 Dec);38.143. https://doi.org/10.47176/mjiri.38.143

Peripheral Arterial Disease is Associated with Sensorimotor Peripheral Neuropathy in People with Type 2 Diabetes

Nahid Hashemi-Madani[1¥], Masoumeh Azadi[2¥], Alireza Khajavi[3], Zahra Emami[1], Mohammad E. Khamseh[1*]

Received: 22 Jul 2024 Published: 7 Dec 2024

Abstract

Background: Micro- and macro-vascular complications of diabetes seem to be interconnected. This study aimed to evaluate the association between peripheral arterial diseases (PAD) and diabetic sensorimotor peripheral neuropathy (DSPN).

Methods: This cross-sectional study was conducted among 748 people with type 2 diabetes (T2DM) referred to a tertiary care center between 2017 and 2022. PAD was defined as Ankle-brachial index (ABI) ≤ 0.9. Loss of protective sensation (LOPS) was applied for the detection of DSPN. Logistic regression analysis was used to determine the association between PAD and DSPN.

Results: The mean age of the participants was 59.6 (±8.8) years, and the median duration of diabetes was 10 (5-16) years. LOPS was detected in 491 individuals (65.6%). ABI ≤ 0.9 was associated with a significantly higher risk of LOPS (OR: 3.65, 95% Confidence Interval (CI): 1.97- 6.74). In addition, every 0.1 decrease in ABI increased the risk of LOPS by 21% (95%CI: 10- 34%). Toe brachial index (TBI) ≤0.7 was also associated with a significantly higher risk of LOPS (OR: 1.77, 95%CI: 1.28- 2.46). Each 0.1 decrease in TBI increased the risk of LOPS by 19% (95%CI: 10- 28%).

Conclusion: PAD is strongly associated with DSPN. Assessment of DSPN could be considered in the presence of PAD.

Keywords: Peripheral artery disease, Diabetes, Sensorimotor peripheral neuropathy, Ankle-brachial index, Loss of protective sensation

Conflicts of Interest: *None declared*
Funding: *None*

This work has been published under CC BY-NC-SA 4.0 license.
Copyright© Iran University of Medical Sciences

Cite this article as: Hashemi-Madani N, Azadi M, Khajavi A, Emami Z, Khamseh ME. Peripheral Arterial Disease is Associated with Sensorimotor Peripheral Neuropathy in People with Type 2 Diabetes. *Med J Islam Repub Iran.* 2024 (7 Dec);38:143. https://doi.org/10.47176/mjiri.38.143

Introduction

Diabetic sensorimotor peripheral neuropathy (DSPN) is the most prevalent micro-vascular complication of diabetes (1, 2). It is the main risk factor for foot ulcers and a leading cause of lower limb amputation in people with type 2 diabetes (T2DM) (3). Moreover, DSPN, foot ulcer, and limb amputation are associated with a reduced quality of life, loss of working time, and eventually an increased risk of mortality (4, 5).

However, despite these devastating outcomes, a large number of patients with DSPN are asymptomatic and remain undiagnosed; thus, it is recommended that patients with diabetes undergo an annual foot examination(6). Assessment of DSPN is a challenging issue. Instruments used for screening and diagnosis of DSPN are time-consuming questionnaires that should be performed by trained practitioners. Moreover, they only provide a probable diagnosis. The most widely used instrument is the Michigan Neuropathy Screening Instrument Questionnaire (MNSIQ; 15-item self-administered questionnaire) (7). However, this instrument has some limitations leading to under-diagnosis of DSPN (8). American diabetes association (ADA) recommends assessing loss of protective sensation (LOPS) in patients with diabetes (9). This included assessment of either temperature perception or pinprick

Corresponding author: *Dr Mohammad E. Khamseh, khamseh.m@iums.ac.ir*

¥: Nahid Hashemi-Madani and Masoumeh Azadi contributed equally to this work as the first authors.

1. Endocrine Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Iran
2. Endocrine Research Center, Institute of Endocrinology and Metabolism, Department of Internal Medicine, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
3. School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

↑What is "already known" in this topic:
It has already been shown that peripheral neuropathy may be more advanced due to peripheral arterial disease (PAD) in diabetic patients.

→What this article adds:
The present study quantified the association of PAD and neuropathy, highlighting the co-existence of micro-and macrovessel disease which has the potential to change the diagnostic and therapeutic approaches.

[Downloaded from mjiri.iums.ac.ir on 2026-11-09]

[DOI: 10.47176/mjiri.38.143]

(small fiber function) and vibration perception using a 128-Hz tuning fork (for large-fiber function) (9). In addition, all patients should undergo 10-g monofilament testing for identification of feet at risk of ulceration and amputation (9). However, these tests are mainly operator-dependent which can lead to false results.

On the other hand, the pathophysiological mechanisms of DSPN are complex and are not fully explained by a single model. Along with the hyperglycemia-induced cellular injury, probably known as the most important factor in DSPN, other factors such as endothelial injury and vascular dysfunction contribute to cellular dysfunction and death (10). Moreover, it seems that micro and macrovascular complications of diabetes are strongly interconnected and may progress simultaneously as a continuum (11, 12). Additionally, indirect evidence demonstrated an association between ankle-brachial index (ABI) and DSPN (13-15).

Thus, we conducted this study to further evaluate the association between LOPS and ABI/ toe brachial index (TBI).

Methods

Study population

This is a cross-sectional study conducted on a population of Iranian people with T2DM who concord with the criteria for assessment of peripheral neuropathy and PAD according to the ADA guideline (9). Data were extracted from the medical records of patients referred to the foot clinic at a tertiary care center in Tehran, Iran, from 2017 to 2022.

Data collection

For this study, all demographic, clinical, and laboratory data, as well as results on the assessment of neuropathy and vascular assessments, were extracted from the patient's medical records. Assessments of diabetic foot at this center are summarized as follows.

Demographic and clinical data

Patients referred to the foot clinic are asked to complete a questionnaire including data on sex, age, duration of diabetes, smoking status, medical history (cardiovascular disease, foot ulceration), and drug history. Blood pressure, weight, and height are measured by an experienced nurse, and body mass index (BMI) is calculated.

Assessment of neuropathy

To identify LOPS, the following examinations are performed: a 10-g-monofilament test, vibration perception, pinprick, temperature perception, and ankle reflex (9). The 10-g monofilament at four points (1st, 3rd, and 5th metatarsal heads and plantar surface of distal hallux) is performed on each foot. The 128 Hz tuning fork is applied over the tip of the great toe bilaterally to assess vibration perception. Ankle reflexes are tested while the patient is resting on the couch. Pinprick test is performed using a disposable pin, which is applied just proximal to the toenail on the dorsal surface of the hallux. The presence of any abnormal test is considered as having LOPS.

Vascular assessment

Vascular assessment is based on ABI and TBI measured using a Doppler ultrasound device (Dopplex Ability (DR5), Huntleigh Healthcare, Cardiff, UK). Before the examination, the participants are asked to avoid caffeine, smoking, and exercise to prevent influencing pressure measurements. Moreover, room temperature is monitored with a thermometer to be maintained between 23◦C and 25◦C to prevent vasoconstriction of digital arteries. ABI ≤ 0.9 is considered as PAD (16).

Statistical analysis

The continuous variables were described using mean (standard deviation (SD)) or median (interquartile range (IQR)), depending on their distribution. Correspondingly, the t-test and Mann-Whitney test were used in these cases. The number (percentage) was used for discrete variables, and the Chi-squared test was applied to them. As the response variable of neuropathy was binary, the logistic regression models were fitted on it. Odds ratios (ORs) are reported both crudely and after adjustment with the main confounders namely age, sex, smoking, CVD (Cardiovascular Disease), Low-density lipoprotein (LDL), and Glycated Hemoglobin (HbA1C). The rationale behind the selection of specific variables for adjustment in the regression models is that they are reported as the major risk factors for the development of peripheral neuropathy in patients with T2DM (17, 18).

Results

This cross-sectional study included 748 patients with T2DM, of whom 491 individuals (65.6%) had LOPS. Table 1 demonstrates the baseline characteristics of the participants. Compared to the patients without LOPS, those who had LOPS were older (60.42 ± 8.97 vs. 58.00± 8.23 ys; P <0.001), more likely to be men (50.5% vs. 31.5%; p < 0.001), and more likely to be ever smoker (13.1% vs. 5.5%; P < 0.001). Patients with LOPS were more likely to have a history of CVD (38.4% vs. 18.4%; P < 0.001) and previous foot ulceration (9.4% vs. 1.2%; P < 0.001); they also were more likely to use insulin (42.9% vs. 31.5%; p 0.003) and anti-hypertensive medications (51.4%vs 38.1%; P < 0.001), but less likely to use statin (79.2% vs. 86.8%; P < 0.011), compared to those with no LOPS. Moreover, patients with LOPS showed significantly higher levels of LDL (79.26±31.90 vs 74.32 ± 30.40 mg/dl; P 0.046) and lower levels of ABI (1.02 ± 0.22 vs. 1.07±0.12; P < 0.001) and TBI (0.69 ± 0.24 vs. 0.78± 0.16; P < 0.001), compared to the individuals without LOPS. In addition, a significantly higher percentage of patients with LOPS presented with ABI ≤ 0.9 (18.3%vs 5.8%; P < 0.001) and TBI ≤ 0.7 (48.5%vs 32.7%; P < 0.001), compared to those with no LOPS. Moreover, of 235 patients who presented with normal ABI (0.9 < ABI <1.3) but low TBI (TBI ≤ 0.7), 69.4% (N = 163) were diagnosed to have LOPS.

[Downloaded from mjiri.iums.ac.ir on 2026-11-09]

[DOI: 10.47176/mjiri.38.143]

Table 1. Baseline characteristics of the participants

Variable	Patients with no LOPS N=257	Patients with LOPS N=491	*P*-value
Age (yr) *	58.00 (8.23)	60.42 (8.97)	<0.001
Sex (%M)	81 (31.5 %)	248 (50.5 %)	<0.001
BMI (kg/m^2) *	28.93 (4.56)	28.77 (4.54)	0.648
Duration of DM (yr) #	10 (5-15)	10 (5-18)	0.281
Ever smoker (%)✞	14 (5.5 %)	64 (13.1 %)	0.001
SBP (mmHg) *	128.34 (17.64)	127.52 (16.89)	0.538
DBP (mmHg) *	78.45 (9.39)	79.11 (9.49)	0.364
CVD (%)✞	47 (18.4 %)	188 (38.4 %)	<0.001
Previous foot ulcer (%)✞	3 (1.2 %)	46 (9.4 %)	<0.001
Insulin users (%) ✞	81 (31.5 %)	210 (42.9 %)	0.003
Statin users (%)✞	223 (86.8 %)	388 (79.2 %)	0.011
ASA users (%)✞	180 (70.0 %)	332 (67.8 %)	0.523
Anti-hypertensive users (%)✞	98 (38.1 %)	252 (51.4 %)	0.001
HbA1C (%)*	7.68 (1.66)	7.92 (1.82)	0.078
LDL (mg/ml) *	74.32 (30.40)	79.26 (31.90)	0.046
HDL (mg/ml) *	46.46 (12.46)	45.85 (11.57)	0.521
TG (mg/ml) *	140.00 (75.23)	152.01 (89.40)	0.071
Chol (mg/ml) *	141.94 (32.73)	147.43 (37.55)	0.053
Cr (mg/ml) *	1.04 (0.61)	1.15 (0.80)	0.063
TBI (mean) *	0.78 (0.16)	0.69 (0.24)	<0.001
ABI(mean) *	1.07 (0.12)	1.02 (0.22)	<0.001
TBI ≤ 0.7 ✞	84 (32.7 %)	238 (48.5 %)	<0.001
ABI≤ 0.9✞	15 (5.8 %)	90 (18.3 %)	<0.001

LOPS: peripheral sensory neuropathy
Data are presented as mean(SD)*, or median (IQR)#, or number (%)✞

Results of regression analyses indicated that ABI ≤ 0.9 was significantly associated with a higher risk of LOPS (OR: 3.65, 95% Confidence Interval (CI): 1.97- 6.74), considering the possible confounders. Moreover, each 0.1 decrease in ABI was associated with a significantly higher risk of LOPS (OR: 1.21, 95%CI: 1.10- 1.34), after adjustment with the possible risk factors. In addition, TBI ≤ 0.7 was significantly associated with a higher risk of LOPS (OR: 1.77, 95%CI: 1.28- 2.46), considering the possible confounders. Moreover, each 0.1 decrease in TBI was associated with a significantly higher risk of LOPS (OR: 1.19, 95%CI: 1.10- 1.28), after adjustment with the possible risk factors (Table 2).

We further analyzed the association between ABI/TBI and individual components of DSPN. The results showed ABI ≤ 0.9 is associated with a significantly higher risk of abnormal individual tests, including pinprick (OR: 1.94, 95%CI: 1.26- 2.98), temperature perception (OR: 7.11, 95%CI: 3.48- 14.53), and ankle reflex (OR: 2.00, 95%CI: 1.30- 3.07), considering all possible risk factors. Moreover, TBI ≤ 0.7 was associated with a significantly higher risk of abnormal individual tests including vibration perception (OR: 1.55, 95%CI: 1.14- 2.12), pinprick (OR: 1.64, 95%CI: 2.20- 1.24), temperature perception (OR: 1.98, 95%CI: 1.44- 2.71), and ankle reflex (OR: 1.79, 95%CI: 1.32- 2.42), adjusting with all possible risk factors (Figure 1).

Table 2. Logistic regression analyses for the association between ABI/TBI and peripheral sensorimotor neuropathy

Variables	Presence of LOPS OR (95%CI)	*P*-value
Continuous ABI (0.1 decrease)		
Non-adjusted	1.19 (1.09,1.30)	<0.001
Adjusted	1.21(1.10,1.34)	<0.001
ABI≤ 0.9 (vs> 0.9)		
Non-adjusted	3.62(2.05,6.40)	<0.001
Adjusted	3.65(1.97,6.74)	<0.001
Continuous TBI (0.1 decrease)		
Non-adjusted	1.21(1.13,1.31)	<0.001
Adjusted	1.19(1.10,1.28)	<0.001
TBI ≤ 0.7 (vs> 0.7)		
Non-adjusted	1.94(1.41,2.66)	<0.001
Adjusted	1.77(1.28,2.46)	0.001

Adjusted for age, sex, smoking, CVD, LDL, and HbA1C

We also investigated the association between different categories of ABI and LOPS. The percentage of patients in each category was as follows: ABI≤.0.9; in 14.02%, 0.9<ABI≤1; in 26.57%, 1<ABI≤.1.1; in 23.36%, 1.1<ABI≤1.3: in 33.24%, and ABI >1.3; in 2.80%. The results indicated that compared to the patients with ABI ≤ 0.9, those with higher ABIs were less likely to develop LOPS [0.9 < ABI ≤ 1 (OR:0.37, 95%CI:0.19-0.72), 1 < ABI ≤ .1.1 (OR:0.26, 95%CI:0.14-0.50), 1.1 < ABI ≤ 1.3 (OR: 0.26, 95%CI: 0.14-0.49)] except for those with ABI >1.3 who shows no difference in development of LOPS (OR:1.38, 95%CI:0.27-7.12), considering all possible risk factors (Figure 2).

Discussion

We found that PAD is significantly associated with an increased risk of LOPS in people with T2DM. Beyond as an indicator of PAD, ABI is also well-known as an indicator of cardiovascular disease (CVD) (19, 20). Moreover, several studies have recently investigated the association between ABI and microvascular complications of diabetes (13, 21). A cohort study conducted on 34689 patients with T2DM demonstrated a U-shape correlation between ABI categories and incidence of microvascular complications of diabetes with the lowest rate in patients with normal

[Downloaded from mjiri.iums.ac.ir on 2026-11-09]
[DOI: 10.47176/mjiri.38.143]

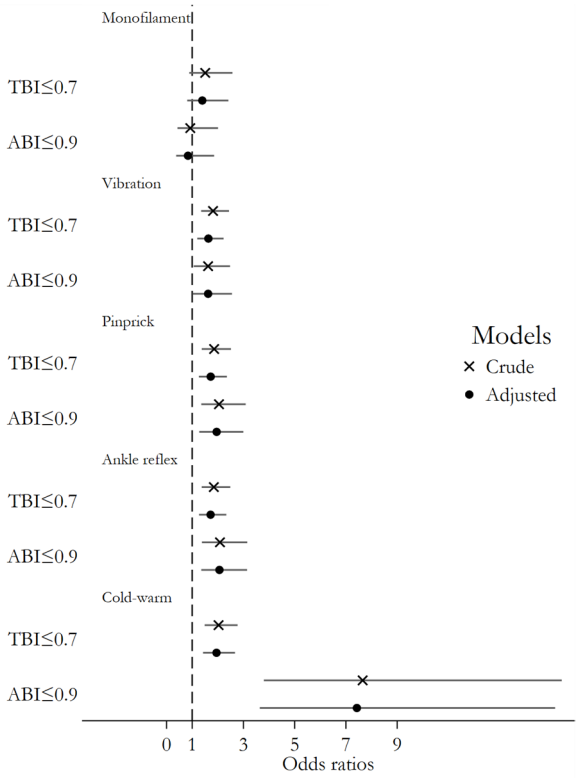

Figure 1. Logistic regression for the association between ABI/TBI and individual components of LOPS.

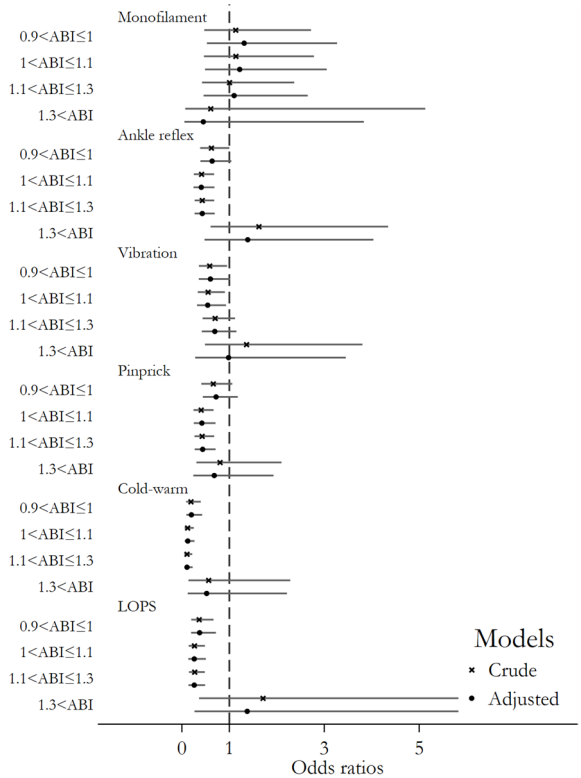

Figure 2. Logistic regression analyses to indicate the risk of abnormal components of LOPS among the different ABI categories. Taking persons with ABI ≤ 0.9 as the reference group.

ABI (1.1 < ABI ≤ 1.3) and the highest rate in ABI ≤ 0.9 and ABI > 1.3 (13). Similarly, we found that compared to ABI ≤ 0.9, the normal ABI categories are associated with a lower risk of LOPS, while there was no difference in the risk of LOPS between low (ABI ≤ 0.9) and high ABI (ABI > 1.3) categories. We further found a significant association between low ABI/TBI and some individual components of LOPS. Additionally, our study indicated that ABI/TBI either as a categorical factor or as a continuous variable, is associated with a higher risk of LOPS.

Based on the studies demonstrating common pathways for the development of macro-and microvascular complications in diabetic patients, it has aroused that they might not be distinct entities (22, 23). Some studies demonstrated PAD is significantly associated with a higher risk of neuropathy and nephropathy (24). More recent studies investigated the connection between small vessel diseases of the brain, kidney, and retina and concluded changes in cerebrovascular bed are significantly associated with alterations in renal and retinal vasculature (25, 26). Moreover, not only did some investigators show that microvascular diseases are associated with an excess risk of heart failure (HF) but also highlighted a trend toward worsening HF outcomes with increasing numbers of micro-vascular diseases (27, 28). The connection of changes between different organs has the potential to be applied to early diagnostic and therapeutic approaches.

Therefore, the robust association that we found between ABI/TBI and LOPS could be a signal favoring the potential use of ABI/TBI for the prediction of neuropathy. Similarly, a study by Alves-Cabratosa et al. concluded that ABI could be used to optimize preventive interventions for both micro-and-macro-vascular complications of diabetes (13). Another study evaluated the prognostic significance of ABI in patients with T2DM and indicated low ABI is associated with the development or progression of neuropathy (29). On the other hand, different methods applied for screening DSPN are of various limitations. The answers to the questionnaires might be confusing or misinterpreted, leading to misdiagnosis (8). Quantitative screening tests, recommended by ADA, lack the objectivity of nerve conduction studies and can be affected by distraction, mental fatigue, and drowsiness of the patients (30). Furthermore, these tests are not sufficient to diagnose the asymptomatic early stages of DSPN (31). In such a challenging situation, risk stratification is helpful for early assessment of high-risk patients. This study provides evidence that ABI/TBI could be considered as predicting factors of neuropathy.

On the other hand, there is no consensus on the measurement of ABI/TBI in patients who have no signs and symptoms of PAD (32, 33). Moreover, TBI is only recommended to be performed in patients with ABI>1.3 suspected to be affected by medial arterial calcification (32). The presence of LOPS in 69.45 of patients who presented with normal ABI but low TBI highlighted the issue that TBI could be considered a risk factor for neuropathy even when ABI is normal. Moreover, a recent study indicated over two-thirds of diabetic patients with low TBI in the presence of normal ABI developed PAD (34). These studies provide evidence that the main problems of diabetic foot, including PAD and neuropathy, may be overlooked by current screening methods. Thus, ABI/TBI should be more widely used in the routine clinical management of

[Downloaded from mjiri.iums.ac.ir on 2026-11-09]

[DOI: 10.47176/mjiri.38.143]

individuals with T2DM, not only in those with signs or symptoms suggesting PAD, as currently recommended. Moreover, TBI could be considered the preferable modality for prediction of PAD and neuropathy in these patients.

Strengths and limitations

Although several studies reported the association between low ABI and neuropathy, we further included patients with ABI > 1.3. Moreover, we evaluated the association between TBI and neuropathy, which, to the best of our knowledge, has not been considered in previous studies. Furthermore, we analyzed data considering ABI/TBI as both categorical and continuous variables. Additionally, this study included a relatively adequate sample size with a low rate of missing data. However, this was a cross-sectional study precluding us from drawing causal inferences. Moreover, as the study was performed in a tertiary care center for diabetic patients, it merely includes the patients referred by the physicians to be screened for neuropathy and PAD. Thus, patients with diabetes suffering from advanced complications of diabetes may not have been included in this sample. Regarded as a selection bias, these issues may limit the generalizability of the current study's findings.

Conclusion

In conclusion, our study demonstrated that ABI, either analyzed as a continuous or as a categorical variable, is a strong risk factor for neuropathy defined as LOPS. We also found no difference in the risk of LOPS between low (ABI ≤ 0.9) and high (ABI > 1.3) ABI groups highlighting the clinical significance of these high-risk groups. Similar to ABI, TBI both as a continuous and categorical variable, is associated with a higher risk of LOPS. Moreover, a subgroup of patients with normal ABI but low TBI indicated a higher risk of LOPS. The strong association between ABI/TBI and LOPS found in this study provided evidence regarding the issue that ABI/TBI can be applied to improve the screening of DSPN.

Authors' Contributions

M.E.K and N.H.M. contributed to the study design. M.A., Z.E., A.K., and N.H.M., contributed to the data acquisition and analysis. N.H.M., M.A., and M.E.K. contributed to the data interpretation. A.K. cleaned and analyzed the data. M.A., A.K., N.H.M., and M.E.K. drafted or substantially contributed to revising the work. All authors read and approved the manuscript.

Ethical Considerations

This study was approved by the Ethics Committee of the Iran University of Medical Sciences. (approval code IR.IUMS.REC.1402.012).

Acknowledgment

Declared none.

Conflict of Interests

The authors declare that they have no competing interests.

References

1. Sun J, Wang Y, Zhang X, Zhu S, He H. Prevalence of peripheral neuropathy in patients with diabetes: A systematic review and meta-analysis. Prim Care Diabetes. 2020;14(5):435-44.
2. Kirthi V, Perumbalath A, Brown E, Nevitt S, Petropoulos IN, Burgess J, et al. Prevalence of peripheral neuropathy in pre-diabetes: a systematic review. BMJ Open Diabetes Res Care. 2021;9(1):e002040.
3. Margolis DJ, Jeffcoate W. Epidemiology of foot ulceration and amputation: can global variation be explained? Med Clin North Am. 2013;97(5):791-805.
4. Rastogi A, Goyal G, Kesavan R, Bal A, Kumar H, Kamath P, et al. Long term outcomes after incident diabetic foot ulcer: Multicenter large cohort prospective study (EDI-FOCUS investigators) epidemiology of diabetic foot complications study: Epidemiology of diabetic foot complications study. Diabetes Res Clin Pract. 2020;162:108113.
5. Tesfaye S, Boulton AJ, Dickenson AH. Mechanisms and management of diabetic painful distal symmetrical polyneuropathy. Diabetes Care. 2013;36(9):2456-65.
6. American Diabetes Association Professional Practice Committee. 12. Retinopathy, neuropathy, and foot care: Standards of Medical Care in Diabetes—2022. Diabetes Care. 2022;45(Supplement_1):S185-S94.
7. Feldman EL, Stevens M, Thomas P, Brown M, Canal N, Greene D. A practical two-step quantitative clinical and electrophysiological assessment for the diagnosis and staging of diabetic neuropathy. Diabetes care. 1994;17(11):1281-9.
8. Mete T, Aydin Y, Saka M, Cinar Yavuz H, Bilen S, Yalcin Y, et al. Comparison of efficiencies of michigan neuropathy screening instrument, neurothesiometer, and electromyography for diagnosis of diabetic neuropathy. Int J Endocrinol. 2013;821745.
9. American Diabetes Association. Introduction: standards of medical care in diabetes—2022. Diabetes care. 2022;45(Suppl 1):S1-S2.
10. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, et al. Diabetic neuropathy. Nat Rev Dis Primers. 2019;5(1):41.
11. Orasanu G, Plutzky J. The continuum of diabetic vascular disease: from macro-to micro. J Am Coll Cardiol. 2009;53(5 Suppl):S35-S42.
12. Chawla A, Chawla R, Jaggi S. Microvasular and macrovascular complications in diabetes mellitus: distinct or continuum? Indian J Endocrinol Metab. 2016;20(4):546-51.
13. Alves-Cabratosa L, Comas-Cufí M, Ponjoan A, Garcia-Gil M, Martí-Lluch R, Blanch J, et al. Levels of ankle–brachial index and the risk of diabetes mellitus complications. BMJ Open Diabetes Res Care. 2020;8(1):e000977.
14. Chevtchouk L, Silva MHSd, Nascimento OJMd. Ankle-brachial index and diabetic neuropathy: study of 225 patients. Arq Neuropsiquiatr. 2017;75(8):533-8.
15. Pizzato F, Marques J. Evaluation of Peripheral Arterial Disease as a Development Factor of Peripheral Neuropathy in Diabetic Patients. Endocrinol Metab Syndr. 2017;6(6):281.
16. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2017;69(11):e71-e126.
17. Pfannkuche A, Alhajjar A, Ming A, Walter I, Piehler C, Mertens PR. Prevalence and risk factors of diabetic peripheral neuropathy in a diabetics cohort: Register initiative "diabetes and nerves". Endocr Metab Sci. 2020;1(1-2):100053.
18. Papanas N, Ziegler D. Risk Factors and Comorbidities in Diabetic Neuropathy: An Update 2015. Rev Diabet Stud. 2015;12(1-2):48-62.
19. Davies JH, Kenkre J, Williams EM. Current utility of the ankle-brachial index (ABI) in general practice: implications for its use in cardiovascular disease screening. BMC Fam Practice. 2014;15:69.
20. Gu X, Man C, Zhang H, Fan Y. High ankle-brachial index and risk of cardiovascular or all-cause mortality: a meta-analysis. Atherosclerosis. 2019;282:29-36.
21. Sheen YJ, Li TC, Lin JL, Tsai WC, Kao CD, Bau CT, et al. Association between thermal threshold abnormalities and peripheral artery disease in patients with type 2 diabetes. Medicine. 2018;97(51):e13803.
22. Hejia Z, Cao Y, Fanke M, Xin DQ, Liyang C, Guo X, et al. Exploring the shared molecular mechanism of microvascular and

[Downloaded from mjiri.iums.ac.ir on 2026-11-09]

[DOI: 10.47176/mjiri.38.143]

macrovascular complications in diabetes: Seeking the hub of circulatory system injury. Front Endocrinol. 2023;14:1032015.
23. Paul S, Ali A, Katare R. Molecular complexities underlying the vascular complications of diabetes mellitus–A comprehensive review. J Diabetes Complications. 2020;34(8):107613.
24. Assem M, Mousa S, Abdelhamid A, Amin S, Elsamadony A, El-Sebaee E, et al. The risk of micro and macrovascular disease in Egyptian patients with diabetes and peripheral arterial disease. J Community Hosp Intern Med Perspect. 2021;11(2):216-9.
25. Chojdak-Łukasiewicz J, Dziadkowiak E, Zimny A, Paradowski B. Cerebral small vessel disease: A review. Adv Clin Exp Med. 2021;30(3):349-56.
26. Eriksson MI, Summanen P, Gordin D, Forsblom C, Shams S, Liebkind R, et al. Cerebral small-vessel disease is associated with the severity of diabetic retinopathy in type 1 diabetes. BMJ Open Diabetes Res Care. 2021;9(1):e002274.
27. Kaze AD, Santhanam P, Erqou S, Ahima RS, Bertoni A, Echouffo-Tcheugui JB. Microvascular disease and incident heart failure among individuals with type 2 diabetes mellitus. J Am Heart Assoc. 2021;10(12):e018998.
28. Verma S, Wanner C, Zwiener I, Ofstad AP, George JT, Fitchett D, et al. Influence of microvascular disease on cardiovascular events in type 2 diabetes. J Am Coll Cardiol. 2019;73(21):2780-2.
29. Cardoso CR, Melo JV, Salles GC, Leite NC, Salles GF. Prognostic impact of the ankle–brachial index on the development of micro-and macrovascular complications in individuals with type 2 diabetes: the Rio de Janeiro Type 2 Diabetes Cohort Study. Diabetologia. 2018;61(11):2266-76.
30. Siao P, Cros DP. Quantitative sensory testing. Phys Med Rehabil Clin. 2003;14(2):261-86.
31. Nagaraja B, Manjula J. A study to estimate the occurrence of peripheral neuropathy among asymptomatic type 2 diabetic patients. IJAM. 2020;7(5):835-9.
32. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017;135(12):e686-e725.
33. Abramson BL, Al-Omran M, Anand SS, Albalawi Z, Coutinho T, de Mestral C, et al. Canadian Cardiovascular Society 2022 guidelines for peripheral arterial disease. Can J Cardiol. 2022;38(5):560-87.
34. Manu CA, Freedman B, Rashid H, Winkley K, Edmonds M. Peripheral arterial disease located in the feet of patients with diabetes and foot ulceration demands a new approach to the assessment of ischemia. Int J Low Extrem Wounds. 2022;21(4):397-404.

[Downloaded from mjiri.iums.ac.ir on 2026-11-09]

[DOI: 10.47176/mjiri.38.143]