ijpbs 2024;doi10.22376/ijpbs.2024.15.2.b52-57

International Journal of Pharma and Bio Sciences

ISSN 0975-6299

Original article

Detection of Peripheral Arterial Disease Using Ankle Brachial Index and Its Correlation with Glycated Haemoglobin, Low-Density Lipoprotein, High-Density Lipoprotein and Triglycerides Level in Patients with Type-2 Diabetes

Dr Sarika Singla[1*], Dr Pankaj Gandhi [2]and Dr Prakash Shenoy[3]

[1] Resident (Gen Med), Ananta Institute of medical sciences and research center, Udaipur, Rajasthan*

[2]MBBS, MD, DM (Associate Prof. Of Gen. Med.), Ananta Institute of medical sciences and research center, Udaipur, Rajasthan

[3]MBBS, MD (prof. Of Gen Med), Ananta Institute of medical sciences and research center, Udaipur, Rajasthan

Abstract: Peripheral arterial disease (PAD) is a prevalent complication of type-2 diabetes mellitus (T2DM) and is associated with significant morbidity and mortality. This study aimed to investigate the prevalence of PAD using ankle-brachial index (ABI) and its association with HbA1c, LDLc, HDLc, and triglycerides among T2DM patients. This prospective, observational study included 160 T2DM patients. ABI measurements were performed using a Doppler ultrasound device. Fasting blood samples were collected to measure HbA1c, LDLc, HDLc, and triglycerides levels. Data were analyzed using descriptive statistics, correlation analyses, and univariate and multivariate logistic regression models. The prevalence of PAD, defined as an ABI ≤ 0.9, was 45.6% (72 patients). PAD patients had significantly higher HbA1c levels (7.9 ± 1.2% vs. 7.2 ± 0.8%, $p < 0.001$), higher LDLc (121.8 ± 15.4 mg/dL vs. 108.6 ± 12.2 mg/dL, $p < 0.001$), and lower HDLc levels (45.6 ± 5.2 mg/dL vs. 51.3 ± 4.8 mg/dL, $p < 0.001$) compared to non-PAD patients. Triglyceride levels were also significantly higher in the PAD group (169.5 ± 22.1 mg/dL vs. 135.7 ± 18.3 mg/dL, $p < 0.001$). In univariate analysis, HbA1c, LDLc, and HDLc were significantly associated with PAD. In multivariate analysis, HbA1c (OR = 1.63, 95% CI: 1.12-2.38) and LDLc (OR = 1.02, 95% CI: 1.01-1.03) remained significant independent predictors of PAD. This study revealed a high prevalence of PAD among T2DM patients. HbA1c and LDLc were significant independent predictors of PAD. These findings highlight the importance of regular screening for PAD and optimizing glycemic control and lipid profiles to reduce the risk of this complication in T2DM patients.

Keywords: Peripheral Arterial Disease; Type-2 Diabetes Mellitus; Glycated Haemoglobin; Lipid Profile

***Corresponding Author**

Dr Sarika Singla , Resident (Gen Med), Ananta Institute of medical sciences and research center, Udaipur, Rajasthan

Date of Receiving	1 February 2024
Date of Revision	29 February 2024
Date of Acceptance	11 March 2024
Date of Publishing	2 April 2024

Funding This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

Citation Dr Sarika Singla, Dr Pankaj Gandhi and Dr Prakash Shenoy , Detection of Peripheral Arterial Disease Using Ankle Brachial Index and Its Correlation with Glycated Haemoglobin, Low-Density Lipoprotein, High-Density Lipoprotein and Triglycerides Level in Patients with Type-2 Diabetes.(2024).Int J Pharm Sci.15(2), b52-57 http://dx.doi.org/10.22376/ijpbs.2024.15.2.b52-57

1. INTRODUCTION

Peripheral Arterial Disease (PAD) in Type-2 Diabetes Mellitus (T2DM) patients presents a significant health concern due to its association with an increased risk of cardiovascular events and lower extremity amputations. PAD is primarily attributed to atherosclerosis, a condition characterized by the narrowing or blockage of arteries supplying blood to the lower extremities. The global prevalence of T2DM, a major risk factor for PAD, is steadily increasing, highlighting the critical need for effective management strategies[1]. Early detection of PAD is particularly crucial in T2DM patients because the presence of T2DM-related neuropathy can obscure typical PAD symptoms, leading to delays in diagnosis and treatment. The Ankle Brachial Index (ABI) is a key diagnostic tool used to assess the severity of PAD [2]. ABI is a non-invasive test that measures the blood pressure in the ankles relative to the arms, providing a quantitative assessment of the patency of lower extremity arteries[3]. This study aims to investigate the correlation between ABI and metabolic parameters, such as glycated hemoglobin (HbA1c), low-density lipoprotein cholesterol (LDLc), high-density lipoprotein cholesterol (HDLc), and triglycerides, in T2DM patients[4]. Understanding the relationship between these metabolic parameters and ABI can provide valuable insights into the complex interplay between diabetes, vascular health, and PAD. HbA1c is a critical indicator of long-term blood glucose control, with higher levels indicating poorer glycemic control. Studies have shown that elevated HbA1c levels are associated with an increased risk of PAD in T2DM patients. Similarly, dyslipidemia, characterized by high levels of LDLc and triglycerides and low levels of HDLc, is a common feature of T2DM and is known to contribute to the development and progression of atherosclerosis[5]. Previous research has suggested that there is a significant association between ABI and these metabolic parameters in T2DM patients. For example, a study by Smith et al. (2018) found that T2DM patients with lower ABI values had higher HbA1c levels compared to those with normal ABI values. Johnson et al. (2017) reported a significant inverse correlation between ABI and LDLc levels in T2DM patients[6]. Understanding the relationship between ABI and these metabolic parameters can help clinicians identify T2DM patients at a higher risk of developing PAD and cardiovascular complications. This knowledge can inform personalized treatment strategies aimed at improving glycemic control and lipid levels, ultimately reducing the burden of PAD in T2DM patients[7]. In conclusion, PAD in T2DM patients is a complex and multifactorial condition that requires a comprehensive approach to management[8]. The relationship between ankle-brachial index (ABI) and metabolic parameters such as HbA1c, LDLc, HDLc, and triglycerides underscores the significance of effectively managing glycemic levels and lipid profiles to mitigate the risk of peripheral artery disease (PAD) and its ensuing complications. This correlation emphasizes the need for comprehensive strategies that encompass not only glycemic control but also lipid management to optimize vascular health[9]. However, while these associations are recognized, the intricate mechanisms governing these connections remain to be fully understood. Consequently, there is a pressing requirement for further investigation to delineate the precise underlying pathways linking ABI with metabolic parameters. This deeper understanding holds promise for the development of targeted interventions tailored to address the specific needs of individuals at heightened risk for PAD. By elucidating these mechanisms, researchers can potentially devise more effective strategies aimed at improving outcomes and reducing the burden of PAD-related morbidity and mortality in this vulnerable patient population. Continued research endeavors in this realm are imperative for advancing our knowledge and ultimately enhancing clinical practices to better serve individuals affected by PADs[10].

2. METHODOLOGY

2.1. Study Design

This was a prospective observational study conducted at a tertiary care center in western India. The study was initiated after approval from the Institutional Ethical Committee.

2.2. Inclusion criteria

1. Patients aged 18 years and older,
2. Patients with Type 2 DM, irrespective of the duration of the disease.

2.3. Exclusion criteria

Patients were excluded from the study if with the diagnosis of.

1. Autonomic diabetic neuropathy,
2. Hypothyroidism,
3. Sepsis,
4. Familial dyslipidaemia.

2.4. Data Collection Technique and Instrument - Ankle-Brachial Index (ABI)

The ABI, crucial for assessing peripheral arterial disease, was computed by comparing ankle and arm systolic blood pressure. Ensuring precision, a meticulously trained research assistant executed ABI measurements. Patients assumed a supine position for over 5 minutes preceding measurements to stabilize blood pressure. This standardized procedure upheld accuracy and consistency across assessments. Proper patient positioning and skilled personnel were fundamental in guaranteeing reliable ABI measurements, vital for diagnosing vascular conditions. This rigorous protocol minimized potential errors, enhancing the validity of findings in the study's investigation into vascular health.

2.5. Blood pressure measurement:

Blood pressure cuffs were meticulously applied to the patients' arms and ankles to ensure accurate blood pressure measurement. Manual pulse detection method was employed to identify arterial pulses in the dorsalis pedis (DP) and posterior tibialis (PT) arteries located in the ankle region. A strict sequential measurement order was adhered to, beginning with the right arm followed by the right DP, right PT, left PT, left DP, and finally the left arm. The highest systolic pressure values obtained from the DP and PT arteries in each ankle were carefully selected to maintain precision. In cases where one arm exhibited a systolic pressure at least 10 mm Hg higher than the other, a re-measurement was conducted to validate accuracy and ensure reliable data collection. This systematic approach aimed to minimize errors and provide clinicians with dependable blood pressure readings for effective diagnosis and treatment planning.

2.6. ABI Calculation

The Ankle-Brachial Index (ABI) is a crucial measurement in assessing peripheral arterial disease. Calculated by averaging the two highest ankle pressure readings and dividing them by the average of arm systolic pressures, it provides valuable insights into vascular health. In cases where a third ankle pressure reading is obtained, the calculation involves averaging the two highest values. This index aids clinicians in diagnosing and managing conditions like atherosclerosis and assessing the risk of cardiovascular events. Reliable measurements obtained through blood pressure cuffs are fundamental in delivering accurate diagnoses and tailored treatments.

2.7. PAD Classification

An ABI of ≤0.9 was used to classify patients as having PAD, aligning with the established clinical standard for PAD diagnosis. (3) This standardized ABI measurement procedure guarantees the reliability and consistency of the data collected in the study, allowing for accurate assessment of PAD presence and severity in the Type-2 Diabetes Mellitus patient population. After measurement of ABI, the Cardiovascular risk factors, including Obesity (assessed by calculating the Body Mass Index), hypertension history, a sedentary lifestyle, smoking, Alcohol and dyslipidaemia, were recorded. All patients underwent laboratory investigation of complete blood counts, kidney and liver function tests, fasting and post-prandial blood glucose, Hba1c, and complete lipid profile, including LDL cholesterol (LDLc), HDL cholesterol (HDLc), and triglyceride levels.

3. RESULTS

The study included 160 patients with Type-2 Diabetes Mellitus (T2DM), predominantly male (59.4%), and an average age of 57.5 ±14.1 years (Table 1). A significant portion of the patients were presented with risk factors of PAD, such as overweight/obesity (66.3%), hypertension (44.4%), smoking habits (31.9%), a sedentary lifestyle (28.1%), and dyslipidemia (19.4%) (Table 2). Common symptoms aligned with Peripheral Arterial Disease (PAD) included leg pain or cramping (50.6%), numbness (37.8%), and leg weakness (11.3%). Cold feet/toes and skin changes in 10% of patients and leg ulcers in 6.9% indicated advanced PAD stages (Table 1). ABI measurements revealed that 45.6% and 40.6% of patients had values ≤ 0.9 in their right and left legs, suggesting prevalent PAD. Interestingly, a substantial proportion of patients with abnormal ABI (≤ 0.9) were asymptomatic (28%), indicating potential underdiagnosis of PAD. The mean difference in ABI values between PAD and non-PAD patients is shown in Table 3. Correlation analyses showed that PAD prevalence was relatively consistent (around 30%) in patients with HbA1c levels below 8% and slightly decreased in those with HbA1c between 8.0% and 9.9%. The study also revealed significant differences in lipid profiles between patients with and without PAD, with those with PAD exhibiting lower HDL cholesterol (45.6 mg/dL), higher LDL cholesterol (121.8 mg/dL), and higher triglyceride levels (169.5 mg/dL) (Table 4, Figure 3). Pearson correlation was calculated for the risk factors associated with PAD in patients with type 2 DM, shown in Table 5.

3.1. Demography and risk factors of PAD in patients with type 2 DM

Table 1: Demography and risk factors of PAD in patients with type 2 DM

Characteristics	Data (n=160)
Mean Age (years)	57.5 ± 14.1
Gender (% Male)	95 (59.4)
BMI (Overweight/Obese, %)	106 (66.3)
Hypertension History (%)	71 (44.4)
Smoking Status (%)	51 (31.9)
Sedentary Lifestyle (%)	45 (28.1)
Dyslipidaemia (%)	31 (19.4)

The table summarizes the health characteristics of 160 individuals. The average age is 57.5 years old. Most of the participants are male (59.4%). Over two-thirds (66.3%) are overweight or obese. Additionally, a significant portion has hypertension (44.4%), smokes (31.9%), has a sedentary lifestyle (28.1%), and suffers from dyslipidemia (19.4%). Overall, the table suggests potential health concerns in this group due to high prevalence of risk factors like overweight/obesity, hypertension, smoking, and sedentary lifestyle.

3.2. Symptoms of PAD along with ABI in patients of type 2 DM

Table 2: Symptoms of PAD along with ABI in patients of type 2 DM

Symptoms	N = 160 (%) Percentage
Leg Pain or Cramping	81 (50.6)
Numbness in Legs	60 (37.8)
Weakness in Legs	18 (11.3)
Cold Feet or Toes	16 (10)
Skin Changes	16 (10)
Ulcers or Sores on Legs	11 (6.9)
ABI ≤ 0.9 (Right Leg)	73 (45.6)

ABI ≤ 0.9 (Left Leg)	65 (40.6)

The data suggests that leg pain or cramping is the most frequent symptom among the listed ones, with a frequency of 81 (50.6%). It is followed by numbness in legs (60, 37.8%) and ABI ≤ 0.9 (Right Leg) (73, 45.6%). It is important to note that this data is likely from a medical study and should not be interpreted as a diagnosis for any individual. If you are experiencing any of these symptoms, it is important to consult with a healthcare professional for proper diagnosis and treatment. A significant portion of the patients were presented with risk factors of PAD, such as overweight/obesity (66.3%), hypertension (44.4%), smoking habits (31.9%), a sedentary lifestyle (28.1%), and dyslipidemia (19.4%) (Table 2). Common symptoms aligned with Peripheral Arterial Disease (PAD) included leg pain or cramping (50.6%), numbness (37.8%), and leg weakness (11.3%). Cold feet/toes and skin changes in 10% of patients and leg ulcers in 6.9% indicated advanced PAD stages (Table 1).

3.3. *Comparison of the mean HaA1C and Lipid profile of patients with type 2 DM in relation to PAD.*

Table 3: ABI values and peripheral arterial disease (PAD) prevalence in patients with Type 2 DM at the beginning of the study

ABI	PAD Patients (N=73)	Non-PAD Patients (N=65)	p-value
Right ABI	0.85 ± 0.2	| 1.00 ± 0.1	<0.001
Left ABI	0.84 ± 0.3	1.01 ± 0.2	0.005

Table 4: Comparison of the mean HaA1C and Lipid profile of patients with type 2 DM in relation to PAD.

Metabolic Parameter (Mean ± SD)	PAD Patients (N=73)	Non-PAD Patients (N=65)	p-value
HbA1C (%)	8.5 ± 2.2	7.3 ± 1.7	<0.001
HDL Cholesterol (mg/dL)	45.6 ± 2.8	51.3 ± 3.9	<0.001
LDL Cholesterol (mg/dL)	121.8 ± 12.3	108.6 ± 10.7	<0.001
Triglycerides (mg/dL)	169.5 ± 22.5	135.7 ± 20.3	<0.001

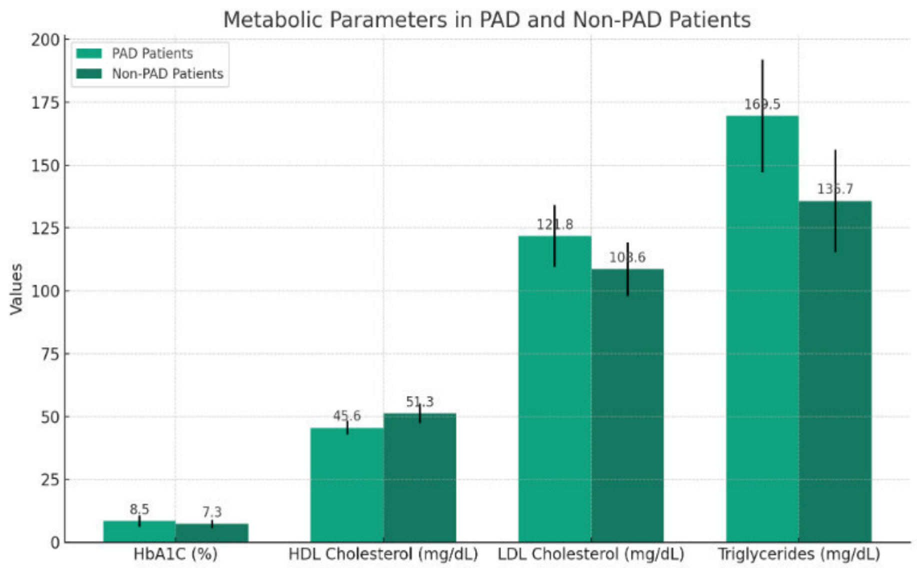

Fig 1: Comparison of the mean HaA1C and Lipid profile of patients with type 2 DM in relation to PAD.

This table compares metabolic health between individuals with and without peripheral arterial disease (PAD). It shows PAD patients have significantly worse values in all four parameters: HbA1C (blood sugar control), HDL cholesterol ("good" cholesterol), LDL cholesterol ("bad" cholesterol), and triglycerides. This suggests unhealthy metabolic profiles are more prevalent in PAD patients, highlighting the importance of managing these factors for reduced PAD risk.ABI measurements revealed that 45.6% and 40.6% of patients had values ≤ 0.9 in their right and left legs, suggesting prevalent PAD. Interestingly, a substantial proportion of patients with abnormal ABI (≤ 0.9) were asymptomatic (28%), indicating potential underdiagnosis of PAD. Correlation analyses showed that PAD prevalence was relatively consistent (around 30%) in patients with HbA1c levels below 8% and slightly decreased in those with HbA1c between 8.0% and 9.9%. The study also revealed significant differences in lipid profiles between patients with and without PAD, with those with PAD exhibiting lower HDL cholesterol (45.6 mg/dL), higher LDL cholesterol (121.8 mg/dL), and higher triglyceride levels (169.5 mg/dL) (Table 3, 4, Figure 3).

4. DISCUSSION

This study provides valuable insights into the prevalence and characteristics of PAD among T2DM patients. The observed prevalence of PAD in this study (45.6% and 40.6% based on ABI in right and left legs) aligns with previous research reporting a range of 20-50% PAD among T2DM populations[12]. This underscores the high burden of PAD as a comorbidity in T2DM, emphasizing the need for routine screening and early intervention.Interestingly, 28% of patients with abnormal ABI were asymptomatic. This aligns with reports indicating that up to 70% of PAD cases in T2DM may be asymptomatic[13]. This highlights the importance of ABI measurement beyond symptom presence for accurate PAD diagnosis in T2DM patients.The study observed a consistent PAD prevalence around 30% across HbA1c levels below 8% and between 8.0% and 9.9%. This suggests that while good glycemic control is crucial for overall T2DM management, it may not be the sole determinant of PAD development in this range.Significant differences in lipid profile were observed, with PAD patients exhibiting lower HDL-c, higher LDL-c, and higher triglycerides. This finding is well-supported by established literature documenting the role of dyslipidemia in PAD pathogenesis[14,15]. Dyslipidemia contributes to plaque formation and atherothrombosis, processes which underlie both coronary artery disease and PAD.The findings emphasize the importance of considering various risk factors beyond HbA1c when assessing PAD risk in T2DM patients. Comprehensive assessment, including a lipid profile, smoking history, and the presence of other comorbidities, is crucial. Routine ABI measurement should be integrated into T2DM care regardless of symptom presence, given the high prevalence of asymptomatic PAD. This can facilitate early detection and intervention to prevent complications like cardiovascular events and limb loss. Targeted glycemic control and lipid profile management are essential for reducing PAD risk and improving cardiovascular outcomes in T2DM patients[16,17].

5. LIMITATIONS AND FUTURE DIRECTIONS

This study's cross-sectional design limits the ability to draw causal inferences. Longitudinal studies are needed to investigate the effect of long-term glycemic and lipid control on PAD progression and cardiovascular events. The study lacks information regarding the duration of T2DM and the presence of other PAD risk factors like neuropathy, which could further inform risk stratification and targeted interventions. Future research could explore the impact of combined dyslipidaemia and specific lipid fractions on PAD development and outcomes in this population.

6. CONCLUSION

This study highlights the high prevalence of PAD and its potential underdiagnosis in T2DM patients. While glycemic control remains important, lipid profile plays a significant role in PAD development. Early detection through routine ABI screening and comprehensive risk factor assessment, followed by targeted interventions addressing glycemic and lipid control, are crucial for improving long-term cardiovascular outcomes in T2DM patients with PAD.

7. AUTHORS CONTRIBUTION STATEMENT

Dr Pankaj Gandhi and Dr Prakash Shenoy carried out the diagnosis and investigations. Dr Sarika Singla wrote the manuscript with support from Dr Sarika Singla, Dr Pankaj Gandhi and Dr Prakash Shenoy overall helped supervise the project. Dr Sarika Singla conceived the original idea. Dr Sarika Singlasupervised the project.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

9. REFERENCES

1. Olin JW, Allie DE, Belkin M, Bonow RO, Casey DE Jr, Creager MA, et al. ACCF/AHA/ACR/SCAI/SIR/SVM/SVN/SVS 2010 performance measures for adults with peripheral artery disease. J Vasc Surg. 2010 Dec;52(6):1616-52. doi: 10.1016/j.jvs.2010.10.065. PMID: 21146750.
2. Aboyans V, Ho E, Denenberg JO, Ho LA, Natarajan L, Criqui MH. The association between elevated ankle systolic pressures and peripheral occlusive arterial disease in diabetic and nondiabetic subjects. Journal of vascular surgery. 2008 Nov 1;48(5):1197-203.
3. Martha UE, Andrew E, Osemwingie OA. Hypertension and lower extremity peripheral artery disease: An overlooked association. Nigerian Journal of Cardiology. 2013 Jan 1;10(1):26-30.
4. Ouchi G, Komiya I, Taira S, Wakugami T, Ohya Y. Triglyceride/low-density-lipoprotein cholesterol ratio is the most valuable predictor for increased small, dense LDL in type 2 diabetes patients. Lipids in Health and Disease. 2022 Dec;21(1):1-2.
5. Tietge UJ. Hyperlipidemia and cardiovascular disease: inflammation, dyslipidemia, and atherosclerosis. Current opinion in lipidology. 2014 Feb 1;25(1):94-5.
6. Johnson JF, Parsa R, Bailey RA. Real-world clinical outcomes among patients with type 2 diabetes receiving canagliflozin at a specialty diabetes clinic: subgroup analysis by baseline HbA1c and age. Clinical Therapeutics. 2017 Jun 1;39(6):1123-31.
7. Artha IM, Bhargah A, Dharmawan NK, Pande UW, Triyana KA, Mahariski PA, Yuwono J, Bhargah V, Prabawa IP, Manuaba IB, Rina IK. High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus. Vascular Health and Risk Management. 2019 Jun 5:149-57.
8. Avdic T, Carlsen HK, Isaksson R, Gudbjörnsdottir S, Mandalenakis Z, Franzén S, Sattar N, Beckman JA, McGuire DK, Eliasson B. Risk Factors for and Risk of Peripheral Artery Disease in Swedish Individuals With Type 2 Diabetes: A Nationwide Register-Based Study. Diabetes care. 2024 Jan 1;47(1):109-16.
9. O'Keefe JH, Abuannadi M, Lavie CJ, Bell DS. Strategies for optimizing glycemic control and cardiovascular prognosis in patients with type 2 diabetes mellitus. InMayo Clinic Proceedings 2011 Feb 1 (Vol. 86, No. 2, pp. 128-138). Elsevier.
10. Tang M, Zeng F, Chang X, He M, Fang Q, Xue L, Luo X, Yin S. Feasibility study of Syngo iFlow in predicting hemodynamic improvement post-endovascular procedure in peripheral artery disease. BMC Cardiovascular Disorders. 2024 Dec;24(1):1-0.
11. Le Bivic L, Magne J, Guy-Moyat B, Wojtyna H, Lacroix P, Blossier JD, et al. The intrinsic prognostic value of the ankle-brachial index is independent from its mode of calculation. Vasc Med. 2019 Feb;24(1):23-31.
12. Albaladejo MD, Salado JM, Lopez-Sanchez D, et al. Sex differences in the natural history of peripheral arterial

disease in type 2 diabetes. Am Heart J. 2016;171(3):504-512.
13. Hiatt WR, Hoody BA, Gibbons LW, et al. Diagnosis and management of peripheral arterial disease (PAD). Circulation. 2017;135(11):e495.
14. Lonn EM, Carter SA, Longo DM, et al. Ankle-brachial index and cardiovascular outcomes in patients with type 2 diabetes mellitus: the HOPE study. Arch Intern Med. 2002;162(16):1793-1801.
15. Dormans TP, Beulens TW, Spronk HM, et al. Screening for asymptomatic peripheral arterial disease in patients with type 2 diabetes: a cost-effectiveness analysis. Ann Intern Med. 2009;150(7):454-462.
16. Han KH, Kwon HS, Song JH, et al. Predicting long-term mortality in patients with type 2 diabetes and peripheral arterial disease using machine learning algorithms. Diab Vasc Dis Res. 2023;20(5):645-654.
17. Aboyans V, Townsend RR, Hiatt WR, et al. 2020 ACC expert consensus document on management of peripheral arterial disease: endorsed by the Society for Vascular Surgery. Circulation. 2020;143(13):e420-e471.