

ORIGINAL RESEARCH

Synergistic Interaction between Older Age and an Abnormal Ankle-Brachial Index in Relation to Diabetic Peripheral Neuropathy



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Abstract

Background: Diabetic peripheral neuropathy (DPN) is associated with older age and an abnormal ankle-brachial index (ABI). However, no previous study has investigated the synergistic interaction between older age and an abnormal ABI in relation to DPN.

Purpose: This study aimed to investigate the independent associations and synergistic interaction of older age and an abnormal ABI in relation to DPN.

Methods: This analytical cross-sectional study included 416 individuals with type 2 diabetes mellitus in Jakarta, Indonesia. Older age was defined as age >64 years. DPN was assessed using a combination of sensory testing with a 10-g Semmes-Weinstein monofilament and vibration testing with a 128-Hz tuning fork, with the diagnosis validated by a physician. ABI was assessed using continuous-wave Doppler ultrasound. Chi-square tests, independent t-tests, and multivariable logistic regression were performed with a significance level of $p < 0.05$.

Results: DPN was identified in 34.9% ($n = 145$) of participants. Older age (adjusted odds ratio [AOR] = 1.74) and an abnormal ABI (AOR = 2.04) were independently associated with DPN. Older participants with an abnormal ABI were 4.03 times more likely to have DPN than adult participants with a normal ABI ($p < .001$). A positive synergistic interaction between older age and an abnormal ABI in relation to DPN was identified (AOR = 4.03; relative excess risk due to interaction [RERI] = 2.20; attributable proportion [AP] = 0.55; synergy index [SI] = 3.65).

Conclusion: Older age and an abnormal ABI were independently and significantly associated with DPN. Older participants with an abnormal ABI showed the most substantial synergistic effect on DPN. These findings highlight the importance of considering age and vascular status in T2DM. Routine ABI assessment, particularly in older adults, may help identify those at greater odds of DPN and guide targeted preventive care.

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1. Introduction

Diabetic peripheral neuropathy (DPN) is a prevalent microvascular complication of diabetes, characterized by progressive damage to peripheral nerve fibers, resulting in neuropathic signs and symptoms (Emara et al., 2025; Zhu et al., 2024). Globally, DPN is present in up to 50% of all individuals with type 1 or type 2 diabetes (Savelieff et al., 2025). A higher prevalence of DPN has been reported in Southeast Asian countries, including Indonesia, Malaysia, and Thailand, at 58%, 54.3%, and 34%, respectively (Malik et al., 2020; Rias et al., 2024).

Individuals with DPN report several symptoms, such as numbness, tingling, diminished motor function, pain, and reduced sensitivity (Chang et al., 2024). This reduced sensitivity increases the odds of developing ulcers and infections, as well as the likelihood of amputation, decreased quality of life, and higher mortality (Papanas, 2020; Perveen et al., 2024). Therefore, identifying factors associated with DPN is crucial for developing preventive strategies and therapeutic interventions to decrease the prevalence of diabetic foot ulcers and amputation (Cheng et al., 2022; Huang et al., 2021).

Surprisingly, age, a non-modifiable factor, is correlated with DPN (Wang et al., 2024). A longitudinal study with a 6-year follow-up found a DPN prevalence of 24% in older age, higher than the 8.4% reported in individuals with diabetes (Wang et al., 2024). In line with previous investigations, older age was independently linked to elevated odds of DPN, with individuals aged ≥ 50 years having 51.2%–85.3% higher odds than those aged < 40 years, and DPN was more prevalent in individuals over 50 years (Pfannkuche et al., 2020). Therefore, estimating the association between age and DPN is crucial. Importantly, the ankle-brachial index (ABI), an indicator of peripheral circulation, is widely used to evaluate vascular health and identify circulatory impairment associated with DPN (Wang et al., 2024).

ABI is a non-invasive vascular measurement that can be measured by comparing the systolic blood pressure at the ankle with that at the brachial artery (Fadlilah et al., 2025; Wang et al., 2024). ABI is a factor associated with DPN, since abnormal ABI values, whether low or high, increase the probability of DPN (Alves-Cabratosa et al., 2020; Fadlilah et al., 2025). In other words, ABI can be a useful, non-invasive measure for detecting DPN and related complications, such as diabetic foot ulcers and the odds of amputation (Cosentino et al., 2020). It can be analyzed as either a continuous or categorical variable and is correlated with the onset or development of DPN. Diabetes is linked to microvascular issues and increased odds of cardiovascular diseases, both of which are connected to a higher incidence of peripheral problems, as reflected in abnormal ABI measurements (Alves-Cabratosa et al., 2020). The relationship between abnormal ABI and DPN among individuals with diabetes, therefore, requires further investigation.

Remarkably, in older age, age-related peripheral stiffness and microvascular dysfunction exacerbate the negative effects of diabetes-induced vascular damage, resulting in diminished peripheral blood flow, as indicated by ABI and heightened nerve ischemia (Gholami et al., 2021). Abnormal ABI indicates underlying vascular pathology, which, when present in older individuals, signifies an association with DPN (Wang et al., 2025). Specifically, abnormal ABI reveals underlying peripheral vascular disease and reduced blood flow resulting from vascular dysfunction, which may affect the supply of oxygen and nutrients to peripheral nerves, leading to persistent ischemia, axonal degeneration, and nerve fiber damage. These pathways contribute to the development of DPN, particularly in older age (Gholami et al., 2021; Wang et al., 2025). Previous investigations have revealed that older age (Wang et al., 2025) and abnormal ABI (Alves-Cabratosa et al., 2020; Fadlilah et al., 2025) are independently linked to the development of DPN. However, the majority of these studies assessed the association of each factor separately. The potential combined or interactive effect of older age and abnormal ABI in relation to DPN has not been adequately investigated. Therefore, the potential mechanisms underlying the synergistic interaction affecting vascular damage may be clarified by exploring the association between older age and abnormal ABI values.

In this study, we hypothesized that the independent and synergistic interaction between older age and abnormal ABI significantly decreases the odds of DPN. Accordingly, the study aimed to investigate the independent and synergistic interactions between older age and abnormal ABI in relation to DPN within the Indonesian population.

2. Methods

2.1 Research design

This analytical cross-sectional study was conducted from July to September 2025 to assess the independent and synergistic interactions between older age and ABI in relation to DPN. Data were obtained at a single point in time from patients with type 2 diabetes mellitus (T2DM) visiting the study sites. This design was adopted to study correlations among variables without asserting causality. Subsequently, this study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) principles (Grech & Eldawlatly, 2024).

2.2 Setting and samples

This study was conducted at two urban hospitals in Jakarta, Indonesia. The study population consisted of patients with T2DM who met the study criteria. Purposive sampling was applied to recruit eligible participants during the study period, an approach that was practically feasible given the study time and resource constraints. Sample size estimation was performed using G*Power 3.1, with an a priori Z-test power analysis for logistic regression. The odds ratio was 1.5,

alpha was 0.05, and power was 0.85 (Zhu et al., 2018). A minimum required sample size of 358 was determined by this estimation. Thus, a total of 416 participants were recruited for this study. Eligibility criteria included being Indonesian, aged 17 years or older, having a T2DM diagnosis as verified by medical practitioners, having fasting plasma glucose > 126 mg/dL, and having no dementia diagnosis. Meanwhile, those who had undergone amputation, were pregnant, had diabetic foot ulcers, had auditory or vision issues, or were unable to speak or communicate were excluded.

2.3 Measurement and data collection

Research assistants, who were bachelor's-level nurses working at the research settings, completed the data collection. Prior to data collection, the researchers and research assistants convened for a meeting and training session to develop a shared understanding of the goals and data collection methods. This activity aimed to ensure that the entire research process complied with the standard operating procedures.

Demographic and behavioral forms. Demographic and behavioral forms inquired about participants' gender, age, occupation, smoking status, diabetes duration, and compliance with the recommended therapy (Rias et al., 2021; Rias et al., 2020).

Physical examination. Biological measures of BMI, ABI, blood pressure, and DPN were obtained (Rias et al., 2020; Fadlilah et al., 2025; Kim et al., 2020). BMI was calculated by dividing body weight (kg) by the square of height (m²). The calculated BMI was then classified into two categories, namely non-obese (BMI < 25 kg/m²) and obese (BMI ≥ 25 kg/m²) (Rias et al., 2020).

ABI was measured using a blood pressure cuff and continuous-wave Doppler ultrasound with an 8-MHz probe to assess lower-extremity perfusion. Participants were measured in the supine position after resting for five minutes. To calculate ABI, we divided the systolic pressure at the ankle by the systolic pressure at the brachial artery. For each leg, we subsequently divided the higher of the two ankle systolic pressures by the higher of the two brachial systolic pressures to ascertain the right and left ABI values (American Diabetes Association, 2023). ABI values were classified as either normal (1.0–1.4) or abnormal (1.0 < ABI > 1.4) (Fadlilah et al., 2025).

Blood pressure was measured using a digital sphygmomanometer. The results were reported as systolic blood pressure (SBP) and diastolic blood pressure (DBP). According to the Eighth Joint National Committee (JNC 8), hypertension was defined as a blood pressure of ≥ 140/90 mmHg, while a blood pressure < 140/90 mmHg was classified as non-hypertensive (Kim & Kim, 2022). The digital blood pressure monitor was calibrated before data collection to ensure accuracy. Calibration was carried out by comparing the instrument readings with those of a reference mercury sphygmomanometer using recognized validation protocols. The device was deemed satisfactory when the measurement discrepancy was within ±3 mmHg, aligning with commonly accepted accuracy requirements.

Participants were instructed to rest in a supine position for at least 5–10 minutes before measurement. Blood pressure measurements were obtained from both arms and both ankles. Brachial systolic pressure was measured in both the right and left arms. For ankle measurements, the cuff was placed just above the malleolus, and systolic pressures were assessed in both legs using Doppler at the dorsalis pedis and posterior tibial arteries. During each measurement, the cuff was inflated until the arterial signal disappeared and then deflated slowly (2–3 mmHg per second).

DPN evaluation encompassed two modalities, i.e., sensory and vibratory assessments, validated by a physician. Previous research indicated that utilizing a minimum of two assessments enhanced sensitivity and specificity for identifying peripheral neuropathy, with positive results occurring if at least one assessment revealed aberrant findings (Fadlilah et al., 2025). Sensory evaluation was performed using the 10-g Semmes-Weinstein Monofilament (SWM) test, which had a reported sensitivity of 69.23% and specificity of 20.0%. Foot sensitivity was classified as normal (sensation in ≥ 5 areas) or abnormal (sensation in < 5 locations). Examined areas included the front, back, and sides of the foot, as well as the metatarsal heads, toes, heel, and the space between the first and second toes on the dorsal side of the foot. The foot sensitivity index was the minimum value of the two feet (Fadlilah et al., 2025). Moreover, vibration was detected using a 128-Hz tuning fork with 76.0% sensitivity and 77.0% specificity (Chattopadhyay et al., 2024). Vibration sense was abnormal if it was not perceived at least at one site. The lowest vibration value of the two feet was used in the study (Fadlilah et al., 2025).

Biochemical examination. Following eight hours of fasting, all respondents were invited to undergo an evaluation of blood glucose control using a fasting blood sample (3–5 mL), which was collected from an antecubital vein and analyzed using an XP-100 automated hematology cell counter. For the present investigation, fasting plasma glucose was defined as categorical data with a controlled glycemic target achieved when the fasting plasma glucose level was within 80–130 mg/dL. Thus, an uncontrolled glycemic target was defined as a fasting plasma glucose level below 80 mg/dL or above 130 mg/dL ([American Diabetes Association, 2023](#)).

2.4 Data analysis

Descriptive statistics were used to summarize demographic and behavioral characteristics, BMI, ABI, blood pressure, and FBG among participants. Continuous variables were presented as means $\pm$ standard deviation, and categorical variables were presented as frequencies (f) and percentages (%). Comparisons between participants with and without DPN were analyzed using an independent t-test for continuous variables and a Chi-square test for categorical variables.

According to the data normality assessment, the Z-scores for skewness and kurtosis were less than 3.29 ([Kim, 2013](#); [Rias et al., 2020](#)); specifically, the skewness value was 0.91, and the kurtosis value was 1.07. This study found a maximum variance inflation factor (VIF) of 1.23, and a score below 10 indicated the absence of multicollinearity ([Kyriazos et al., 2023](#)). The adjusted odds ratios (AORs) for DPN were calculated using multivariate logistic regression, adjusting for potential confounders, including diabetes duration, blood pressure, and gender.

Meanwhile, the synergistic effect was calculated using logistic regression, accompanied by 95% confidence intervals (CIs). The formula for measuring the synergistic interaction between older age and ABI in relation to DPN was assessed by establishing four dummy variables corresponding to the following four (2×2) conditions: (1) age with normal ABI (the reference condition or β_1); (2) older age with normal ABI (β_2); (3) age with abnormal ABI (β_3); and (4) older age with abnormal ABI (β_4). The synergistic interaction across the specified categories revealed that (1) $\beta_4 = \beta_3 \times \beta_2$ signified no interaction, (2) $\beta_4 > \beta_3 \times \beta_2$ suggested a positive interaction, and (3) $\beta_4 < \beta_3 \times \beta_2$ denoted a negative interaction ([Kurniasari et al., 2021](#)).

Additive interaction between older age and abnormal ABI in relation to DPN was assessed using the relative excess risk due to interaction (RERI), attributable proportion (AP), and synergy index (SI). Participants were classified into four exposure groups based on age and ABI levels, with those unexposed to both factors as the reference group. Relative risks (RRs) were estimated for each group, and additive interaction was quantified using standard formulas: $RERI = \beta_4 - \beta_2 - \beta_3 + 1$, $AP = RERI / \beta_4$, and $SI = (\beta_4 - 1) / [(\beta_2 - 1) + \beta_3 - 1]$. Evidence of additive synergy was defined as $RERI > 0$, $AP > 0$, and $SI > 1$ ([Kim et al., 2020](#)). The Statistical Package for the Social Sciences, Version 26.0 (Chicago, IL, USA) was used for all statistical calculations. A p -value of less than 0.05 was used to indicate statistically significant differences.

2.5. Ethical considerations

This study received ethical approval from the Ethics Research Committee of Universitas Muhammadiyah Jakarta (Number 137/PE/KE/FKK-UMJ/2025). Each participant provided written informed consent before participating in the survey. To ensure anonymity and protect participant data, all recorded data were assigned research codes, and no personal identifiers were included.

3. Results

3.1. Participant characteristics and clinical factors associated with DPN

Table 1 outlines the demographic characteristics and clinical parameters associated with DPN, along with comparisons between participants with and without DPN. The present study included 416 participants. Participants with DPN were predominantly female ($p < 0.001$), older ($p = 0.001$), non-smokers ($p < 0.001$), hypertensive ($p < 0.005$), had a diabetes duration of < 5 years ($p = 0.048$), and had an abnormal ABI ($p < 0.001$). Further analyses showed no significant differences between the groups in compliance with diabetes therapy, occupation, peripheral oxygen saturation, BMI, and FBG. The proportion of participants with abnormal ABI was higher in the DPN group than in the non-DPN group (**Table 1**).

Table 1. Demographic characteristics of respondents and association with diabetic peripheral neuropathy (DPN)

Characteristics	Total	Diabetic Peripheral Neuropathy (DPN)		<i>p</i> -value ^a
	f (%)	With DPN (n=271) f (%)	Without DPN (n=145) f (%)	
Gender				
Female	252 (60.6)	182 (67.2)	70 (48.3)	< .001*
Male	164 (39.4)	89 (32.8)	75 (51.7)	
Age (years)				
≤ 64	295 (70.9)	207 (76.4)	88 (60.7)	.001*
> 64	121 (29.1)	64 (23.6)	57 (39.3)	
Compliance with diabetes therapy				
Yes	329 (79.1)	217 (80.1)	112 (77.2)	.528
No	87 (20.9)	54 (19.9)	33 (22.8)	
Occupation				
Actively employed	130 (31.3)	79 (29.2)	51 (35.2)	.223
Unemployed	286 (68.8)	192 (70.8)	94 (64.8)	
Hypertension				
No	165 (39.7)	121 (44.6)	44 (30.3)	.005*
Yes	251 (60.3)	150 (55.4)	101 (69.7)	
Smoking				
No	291 (70.0)	208 (76.8)	83 (57.2)	< .001*
Yes	125 (30.0)	63 (23.2)	62 (42.8)	
Peripheral oxygen saturation				
Normal (≥ 95%)	396 (95.2)	261 (96.3)	135 (93.1)	.155
Hypoxemia (< 94%)	20 (4.8)	10 (3.7)	10 (6.9)	
Duration of diabetes diagnosis				
≤ 5 years	243 (58.4)	168 (69.1)	75 (30.9)	.048*
> 5 years	173 (41.6)	103 (59.5)	70 (40.5)	
BMI (kg/m ²)				
< 25	142 (34.1)	100 (36.9)	42 (29.0)	.129
≥ 25	274 (65.9)	171 (63.1)	103 (71.0)	
FBG (mg/dL)				
< 200	216 (51.9)	149 (55.0)	67 (46.2)	.100
≥ 200	200 (48.1)	122 (45.0)	78 (53.8)	
ABI				
Normal (1.0–1.4)	319 (76.7)	222 (81.9)	97 (66.9)	< .001*
Abnormal (1.0 < ABI > 1.4)	97 (23.3)	49 (18.1)	48 (33.1)	

Notes. n = 416. ABI = Ankle-brachial index; BMI = body mass index; FBG = fasting blood glucose; SD = standard deviation. ^a Chi-square test with *p*-value. *Variables with statistically significant differences between the with and without DPN groups (*p* < 0.05).

3.2. Multiple logistic regression of age, gender, blood pressure, smoking status, duration of diabetes, and ABI in relation to DPN

Table 2 presents the results of the multivariate logistic regression analysis of age, gender, blood pressure, smoking, duration of diabetes, and ABI in relation to DPN among participants. After adjustment, older age, hypertension, and abnormal ABI were significantly associated with increased odds of DPN. Older age was associated with 1.74 times higher odds of DPN than younger age (AOR = 1.74, 95% CI = 1.07–2.84, *p* = .027). In addition, participants with abnormal ABI had 2.04-fold higher odds of DPN than those with a normal ABI, after adjustment for compliance with diabetes therapy, occupation, peripheral oxygen saturation, body mass index, and fasting blood glucose (Table 2).

Table 2. Adjusted β coefficients and 95% confidence intervals (CIs) of gender, age, hypertension, smoking, duration of diabetes, and ankle-brachial index for DPN

Variables	Diabetic Peripheral Neuropathy (n = 416)			
	OR (Unadjusted Odds Ratio; 95% CI)	p-value	AOR (Adjusted Odds Ratio; 95% CI)	p-value
Gender				
Female	Ref.		Ref.	
Male	2.19 (1.45-3.31)	<.001*	1.55 (0.86-2.78)	.144
Age (years)				
Age (≤ 64)	Ref.		Ref.	
Older age (> 64)	2.10 (1.34-3.24)	.001*	1.74 (1.07-2.84)	.027*
Hypertension				
No	Ref.		Ref.	
Yes	1.85 (1.21-2.84)	.005*	1.61 (1.01-2.55)	.044*
Smoking				
No	Ref.		Ref.	
Yes	2.38 (1.55-3.64)	<.001*	1.74 (0.95-3.18)	.072
Duration of diabetes diagnosis				
≤ 5 years	Ref.		Ref.	
> 5 years	1.52 (1.01-2.29)	.048*	1.02 (0.64-1.62)	.947
ABI				
Normal (1.0-1.4)	Ref.		Ref.	
Abnormal (1.0 < ABI > 1.4)	2.242 (1.410-3.566)	<.001*	2.04 (1.26-3.31)	.004*

Notes. n=416. ABI = ankle-brachial index; CI = confidence interval. Adjusted β coefficients and 95% CI were estimated using multivariate logistic regression after adjusting for compliance with diabetes therapy, occupation, peripheral oxygen saturation, body mass index, and fasting blood glucose. *Statistically significant.

3.3. Synergistic interaction between age and ABI in relation to DPN

As shown in Table 3, participants who were older and had an abnormal ABI had 4.03-fold higher odds of DPN compared to participants of normal age with normal ABI. Moreover, the combination of older age and an abnormal ABI status in relation to DPN showed a positive synergistic interaction. This was indicated by the formula for synergistic interaction, where the AOR for older age and abnormal ABI was greater than the AOR for younger age and abnormal ABI $\times$ the AOR for older age and normal ABI ($4.03 > 1.43 \times 1.40 = 4.03 > 2.01$), after controlling for potential confounding variables, namely gender, age, hypertension, smoking status, diabetes duration, compliance with diabetes therapy, occupation, peripheral oxygen saturation, body mass index, and fasting blood glucose (Table 3).

The synergistic exposure to older age and abnormal ABI was associated with higher odds of DPN (AOR = 4.03) than older age and normal ABI (AOR = 1.40) or younger age and abnormal ABI (AOR = 1.43). The calculated RERI was 2.20, indicating excess risk attributable to the interaction beyond the sum of the individual effects. The AP due to interaction was 0.55, suggesting that approximately 55% of the risk of DPN among individuals with both exposures was attributable to their interaction. The SI was 3.65, further supporting the presence of an additive synergistic interaction between older age and abnormal ABI in relation to DPN.

4. Discussion

This study provides empirical evidence that the synergistic interaction between older age and abnormal ABI significantly elevated the odds of DPN among the Indonesian population. The results suggested that age, diabetes duration, ABI, gender, hypertension, and smoking status were associated with DPN. However, after adjustment using multiple logistic regression, only age, ABI, and hypertension remained significant.

The current findings indicated that 34.9% of participants had DPN. This proportion was lower than those in studies undertaken in Germany (42.2%) (Pfannkuche et al., 2020), China (67.6%) (Wang et al., 2023), and Mali (69.8%) (Maiga et al., 2020). However, it was higher than that reported in a study in Malaysia (26.5%) (Ching et al., 2024). The global variability in the

prevalence of DPN might be attributed to several factors, including regional characteristics, diagnostic criteria, timing of diagnosis, prompt initiation of treatment, diabetes duration, age, body mass index, and glycemic control status (Fadlilah et al., 2025; Owolabi et al., 2022; Wang et al., 2023). The variability in the prevalence of DPN among countries may be affected by diverse regional factors that influence both disease risk and detection. Specifically, demographic factors, encompassing age distribution, diabetes duration, and concomitant conditions, alongside lifestyle elements such as dietary practices and physical activity, may influence disparities in neuropathy risk. Furthermore, healthcare system variables such as service accessibility, routine screening availability, and early diabetes management can result in underdiagnosis, whereas socioeconomic and educational factors may impact patients' awareness, self-management, and treatment adherence, consequently affecting the long-term burden of DPN (Owolabi et al., 2022; Wang et al., 2023).

Table 3. Synergistic effect of age and ankle-brachial index for diabetic peripheral neuropathy

Variables	With DPN (n=271)	Without DPN (n=145)	OR (Unadjusted Odds Ratio; 95% CI)	p-value	AOR (Adjusted Odds Ratio; 95% CI)	p-value
Both age and normal ABI	171 (63.1)	69(47.6)	Ref.		Ref.	
Both older age and normal ABI	51(18.8)	28(19.3)	1.36 (0.68-2.33)	.263	1.40 (0.77- 2.54)	.277
Both age and abnormal ABI	36(13.3)	20(13.8)	1.38 (0.75-2.54)	.307	1.43 (0.75-2.73)	.276
Both older age and abnormal ABI	13(4.8)	28(19.3)	5.34 (2.61-9.91)	<.001*	4.03 (1.77-9.21)	<.001*

Notes. n = 416. Adjusted β coefficients and 95% CI were estimated using multivariate logistic regression after adjusting for gender, age, hypertension, smoking, duration of diabetes, compliance with diabetes therapy, occupation, peripheral oxygen saturation, body mass index, and fasting blood glucose. Older age (> 64) and age (≤ 64); Abnormal ABI ($1.0 < \text{ABI} > 1.4$) and normal ABI ($1.0-1.4$). *Statistically significant.

We identified a strong age-related increase in the prevalence of DPN. Several investigations have indicated a correlation between older age, diabetes, and DPN (Hicks et al., 2021; Wang et al., 2023). A previous study revealed that individuals aged ≥ 70 years with diabetes had a 1.85-fold elevated odds of developing DPN compared with those aged < 40 years (Wang et al., 2024). Research in China demonstrated that individuals of older age (≥ 60 years) had a 2.05-fold elevated odds of developing DPN compared with those aged < 60 years (Chen et al., 2024). Another study posited that older individuals with diabetes had a fivefold elevated odds of developing DPN compared with younger individuals (Negussie & Bekele, 2024). The following mechanisms may provide pathways linking older age, diabetes, and DPN. To begin with, age-related physiological alterations induce microvascular dysfunction and a reduction in nerve fibers, rendering nerves more susceptible to harm and diminishing their regenerative capacity, hence exacerbating and accelerating DPN development (Wang et al., 2024). Additionally, age-related hypovitaminosis D triggers metabolic dysfunction, oxidative stress, and ongoing low-grade inflammation, all of which contribute to nerve deterioration and the development of diabetic peripheral neuropathy (DPN) in older adults (Dominguez et al., 2024). These mechanisms might enhance our understanding of the pathways through which older age may contribute to DPN.

The current findings demonstrated that abnormal ABI significantly increased the odds of DPN. These results were consistent with a previous cross-sectional study in which both low and high ABI levels were significantly correlated with the incidence of DPN, with odds ratios of 2.73 and 2.19, respectively (Fadlilah et al., 2025). Notably, individuals with diabetes exhibiting high and low ABI levels had 1.44-fold and 2.10-fold higher odds of developing DPN, respectively (Alves-Cabrata et al., 2020). A prevalent connection between DPN and vascular dysfunction in diabetes could lead to diminished blood flow, which might result in nerve injury and DPN development (Wang et al., 2025). Furthermore, low ABI levels lead to reduced blood circulation to the lower limbs and metabolic disruptions in Schwann cells and axons, precipitating nerve loss and neuropathic manifestations (Jakubiak et al., 2020; Zhu et al., 2024). A high ABI level

generally indicates arterial stiffness, preventing sufficient vascular compression (Zhu et al., 2024). This microcirculatory impairment results in variations in tissue oxygenation and heightened oxidative stress and inflammation, ultimately exacerbating peripheral nerve injury (Koumelli et al., 2025). These arguments highlight that low and high ABI levels might compromise the oxygen and nutrient supply to neurons in the peripheral circulation.

To the best of our knowledge, this is one of the few investigations exploring whether older age and abnormal ABI levels synergistically increase DPN. Investigating the links between older age and abnormal ABI could clarify the biological mechanisms underlying the synergistic relationship affecting vascular damage and inflammation. A previous investigation, carried out in a prospective clinical study with a diabetic older adult population, identified a correlation between systemic inflammatory indicators and the onset and progression of neuropathy (Zheng et al., 2021). Elevated inflammatory gene expression in dorsal root ganglion macrophages in DPN exacerbated vascular damage and advanced neuropathy through microvascular malfunction and a heightened inflammatory response. Identifying and regulating these inflammatory pathways might serve as possible therapeutic targets in DPN (Baum et al., 2021). Moreover, a combination of therapies targeting endothelial health and desert hedgehog signalling might offer significant benefits for individuals with diabetes and abnormal ABI, potentially preventing blood-nerve barrier breakdown and DPN progression (Li et al., 2022). Remarkably, older age combined with abnormal ABI was associated with heightened odds of vascular problems among individuals with DPN.

5. Implications and limitations

This study underlined the importance of ABI testing in older adults with diabetes to detect peripheral vascular problems early. To prevent diabetic peripheral neuropathy, nurses should provide routine screening, educate patients on foot care, and promote glycemic management and healthy lifestyles. Comprehensive and effective care planning requires interprofessional collaboration. In older patients with diabetes, it is important to recognize the link between abnormal ABI and DPN. Blood glucose control, foot inspection, early detection of sensory changes, and physician advice can decrease problems and improve quality of life.

The results have several implications for research and clinical practice. The synergistic interaction between older age and abnormal ABI emphasizes the necessity for early and comprehensive vascular-neurological screening in persons with diabetes, especially older adults. ABI measurement during routine evaluations may assist in identifying DPN, allowing for earlier intervention and personalized care. Future researchers should investigate integrative models that incorporate vascular health, aging, and neuropathic development and evaluate preventive strategies for DPN.

Nevertheless, the current investigation has several limitations. To begin with, as a cross-sectional method was applied, causal effects could not be described, resulting in mere speculation on the subject. In addition, we did not rule out the possibility that DPN was influenced by markers of vascular damage or inflammation-associated factors, such as alcohol consumption, oxidative stress markers, or dyslipidemia. However, this investigation controlled for potential confounding variables, including gender, hypertension, diabetes duration, and smoking status. Finally, the purposive sampling method implemented in this study may have generated selection bias, because participants were recruited from only two urban government hospitals, which may restrict the generalizability of the findings. Therefore, further investigations should address the limitations of the current study by including larger sample sizes, longitudinal research methods, and clinical factors to elucidate the association between age, abnormal ABI, and DPN.

6. Conclusion

This study highlights that older age and abnormal ABI are clinically significant factors associated with DPN among individuals with T2DM. It further reports a synergistic interaction between older age and abnormal ABI in relation to DPN within the Indonesian population. It thus underscores the importance of age-related vascular impairment in the development of neuropathic complications. These findings indicate that abnormal ABI may serve as an indicator for detecting individuals at greater odds of DPN, particularly among older adult populations.

From a clinical point of view, it may be possible to identify vascular impairment earlier and guide targeted preventive measures for DPN by integrating routine ABI monitoring into diabetes

management. It is important to tailor diabetes education models and care programs to the unique needs of older adults, taking into account their cognitive, functional, and therapeutic limitations. The effectiveness of vascular examination, age-specific education, and management strategies in preventing and treating DPN can be enhanced by healthcare providers.

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Author contribution

YS contributed to conception, design, acquisition, analysis, interpretation, drafting the manuscript, critically revising the manuscript, giving final approval, and agrees to be accountable for all aspects of the work, ensuring integrity and accuracy. RN contributed to acquisition, analysis, interpretation, drafted the manuscript, critically revised the manuscript, gave final approval, and agrees to be accountable for all aspects of the work, ensuring integrity and accuracy. II contributed to acquisition and interpretation, drafted the manuscript, critically revised the manuscript, gave final approval, and agrees to be accountable for all aspects of the work, ensuring integrity and accuracy. YA contributed to acquisition and interpretation, drafted the manuscript, critically revised the manuscript, gave final approval, and agrees to be accountable for all aspects of the work, ensuring integrity and accuracy. YAR contributed to analysis, interpretation, drafted manuscript, critically revised manuscript, gave final approval, and agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, funding, and/or publication of this article.

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Declaration of Generative Artificial Intelligence (AI)

The authors used artificial intelligence (AI)-assisted tools solely for language editing and grammatical improvement during manuscript preparation. All scientific content, data analysis, interpretation, and conclusions were developed independently by the authors, who take full responsibility for the integrity and accuracy of the manuscript.

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