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Original Article

Evaluating albuminuria as a predictor of subclinical atherosclerosis in type 2 diabetes: a community-based cross-sectional study

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Abstract

The burden of microvascular and macrovascular complications of type 2 diabetes mellitus (T2DM) in Indonesia is increasing. Albuminuria has been proposed as a marker of atherosclerosis, while carotid intima–media thickness (CIMT) is a validated indicator of subclinical atherosclerosis. Evidence from community-based populations in Indonesia remains limited. To assess the association between albuminuria and CIMT in individuals with T2DM. A cross-sectional study was conducted using secondary data from the *PTM Bogor Cohort Follow-Up Study 2019–2020*. Participants with available albumin-to-creatinine ratio (ACR) and CIMT measurements were included. Multivariate analyses adjusted for demographic factors, cardiovascular risk factors, and diabetes-related treatments. A total of 195 participants (mean age 56.9±9.0 years; 76.4% women) were analyzed. Normoalbuminuria, microalbuminuria, and macroalbuminuria were observed in 50.3%, 38.5%, and 11.3% of subjects, respectively. The median CIMT was 0.76 mm, with 39.5% exhibiting elevated CIMT. Albuminuria showed a weak correlation with CIMT (r=0.142; p=0.047). After adjustment, albuminuria was not independently associated with CIMT (p=0.878), whereas age (p=0.004) and hypertension (p<0.001) remained significant. ROC analysis demonstrated poor predictive value of ACR for elevated CIMT (AUC 0.489; p=0.795). Albuminuria was not an independent predictor of increased CIMT after adjustment for confounders. ACR has limited utility as a marker of subclinical atherosclerosis in community-based T2DM populations.

Keywords: albuminuria, carotid intima-media thickness, type 2 diabetes mellitus, atherosclerosis, cardiovascular risk

Introduction

The prevalence of diabetes mellitus (DM) in Indonesia increased from 6.9% in 2013 to 10.9% in 2018. DM-related complications contribute significantly to morbidity and mortality [1, 2]. Long-term complications of DM are categorized into microvascular and macrovascular types. One common microvascular

complication is diabetic nephropathy, characterized by the presence of albuminuria. Diabetic nephropathy is the leading cause of end-stage renal disease requiring renal replacement therapy, affecting approximately 40% of patients with type 1 and type 2 DM. It is defined by increased urinary albumin excretion (UAE) or urinary albumin-to-creatinine ratio (ACR) in the absence of other kidney diseases, and is classified into microalbuminuria (UAE 20–199 µg/min or ACR 30–300 mg/g) and macroalbuminuria (UAE >200 µg/min or ACR >300 mg/g). Diabetic nephropathy is strongly associated with cardiovascular disease (CVD). The CHARM study reported that the presence of micro- or macroalbuminuria increases mortality risk by 60–80%, primarily due to CVD [3–5].

High-resolution B-mode ultrasonography for measuring carotid intima-media thickness (CIMT) has been used effectively to detect subclinical atherosclerosis and predict coronary artery disease and stroke. CIMT is a validated surrogate marker for early atherosclerosis in diabetic patients; however, its use remains limited in many areas of Indonesia [6–10]. A review by Rosenson et al. emphasized the link between microvascular and macrovascular complications in DM and the importance of early microvascular detection for cardiovascular risk assessment [11]. Several studies have reported a positive correlation between albuminuria and CIMT in patients with type 2 DM. Elevated ACR levels were associated with a 1.96 to 2.76-fold increase in CIMT, independent of conventional cardiovascular risk factors, suggesting that albuminuria may serve as an early marker for CVD in type 2 DM [12].

Nevertheless, research exploring the association between diabetic nephropathy or albuminuria and CIMT in community-based diabetic populations in Indonesia is still lacking. No studies have established an optimal albuminuria cut-off value for predicting increased CIMT in this population. This study aims to analyze the association between albuminuria severity and CIMT as a non-invasive approach for early detection of microvascular and macrovascular complications in patients with type 2 DM.

Material and methods

Study design and data collection

This cross-sectional study utilized secondary data from the Evaluation of Chronic Complications of Type 2 Diabetes Mellitus: PTM Bogor Cohort Follow-Up Study 2019–2020, conducted by the Indonesian Ministry of Health and the Faculty of Medicine, Universitas Indonesia. Of the 587 participants with type 2 DM, 99 were excluded due to incomplete data. A total of 195 subjects with available albumin-to-creatinine ratio (ACR) and carotid intima-media thickness (CIMT) measurements were included in the analysis.

Variable measurements

Early morning, first-void urine samples were collected for ACR assessment. Urinary albumin was measured using the immunoturbidimetric method, and urinary creatinine was assessed using the Jaffe kinetic method. ACR was calculated by dividing albumin (mg/dL) by creatinine (mmol/L) and expressed in mg/g.

CIMT was measured by a trained sonographer using a high-resolution B-mode ultrasound with a 7.5–10 MHz linear transducer. Measurements were taken at the far wall of the right and left common carotid arteries, 1.5 cm proximal to the bifurcation, during end-diastole. CIMT was defined as the distance between the lumen-intima interface and the media-adventitia interface. All measurements were validated by experienced cardiologists.

Statistical analysis

Data were analyzed using SPSS version 23 for Windows. A bivariate analysis was conducted to assess the association between albuminuria levels and carotid intima-media thickness (CIMT) using Spearman's correlation. Two-tailed tests were applied with a significance level set at $p<0.05$. Bivariate analyses were also performed to evaluate the association between potential confounders and CIMT. Ordinal categorical variables were analyzed using Spearman's correlation, nominal categorical variables using independent samples t-tests, and continuous variables using Pearson's correlation. Variables with $p<0.25$ in bivariate analyses were included in a multivariable linear regression model. Confounders such as age, sex, smoking status, hypertension, antihypertensive therapy, dyslipidemia, statin use, body mass index (BMI), and diabetes treatment were adjusted in multivariate analysis. Statistical significance was defined as $p<0.05$ (95% confidence level). A Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the discriminative ability of urinary albumin-to-creatinine ratio (ACR, mg/g) in identifying increased CIMT.

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Results

Participant characteristics

A total of 195 subjects were included, with a mean age of 56.9 years (SD 9.02); the majority (39.5%) were aged 51–60 years. Most participants were female (76.4%), and over half had a history of smoking (56.3%), including 17.4% current smokers and 37.9% former smokers. The median duration of diabetes was 8 years (range: 4–29 years). Approximately 41% had received diabetes treatment, while the rest were untreated. Hypertension was reported in 73.3% of subjects, with 67.8% receiving antihypertensive therapy. Dyslipidemia was present in 96.9% of participants, yet only 21.2% were on statin therapy. The mean body mass index (BMI) was 27.7 kg/m^2 (range: 16.8–41.6), with most subjects classified as obese class I (50.3%). The mean systolic blood pressure was 138.7 mmHg (SD 22), and the median diastolic pressure was 84 mmHg (range: 63–136 mmHg). Median HbA1c was 6.8% (range: 4.7–13.9%), indicating relatively good glycemic control. The mean LDL level was 133.4±30.1 mg/dL, and the median triglyceride level was 137 mg/dL. Mean estimated glomerular filtration rate (eGFR) was 75.9±19.8 mL/min/1.73 m^2, suggesting mild renal impairment in some participants. Normal albuminuria was observed in 50.3% of subjects, while 38.5% had microalbuminuria and 11.3% had macroalbuminuria. The median CIMT was 0.76 mm (range: 0.40–1.60 mm), with increased CIMT detected in 39.5% of participants. Detailed baseline characteristics are presented in Table 1.

Relationship between degree of albuminuria and CIMT in Type 2 DM

A Spearman correlation test was conducted to assess the bivariate association between albuminuria grade and carotid intima-media thickness (CIMT) in patients with type 2 diabetes mellitus. As shown

Table 1: Baseline characteristics of study participants (n=195).

Variable	Total (n=195)
Age (years), mean (SD)	56.9 (9.02)
Age group, n (%)	
31–40 years	9 (4.6%)
41–50 years	36 (18.5%)
51–60 years	77 (39.5%)
61–70 years	62 (31.8%)
71–80 years	11 (5.6%)
Sex, n (%)	
Male	46 (23.6%)
Female	149 (76.4%)
Smoking history, n (%)	
Current smoker	34 (17.4%)
Former smoker	74 (37.9%)
Never smoked	87 (44.6%)
Diabetes duration (years), median (range)	8 (4–29)
Diabetes treatment history, n (%)	80 (41.0%)
Hypertension history, n (%)	
Yes	143 (73.3%)
Treated	97 (67.8%)
Untreated	46 (32.2%)
No	52 (26.7%)

Table 1: Continued.

Variable	Total (n=195)
Dyslipidemia history, n (%)	
Yes	189 (96.9%)
On statins	40 (21.2%)
No statin treatment	149 (78.8%)
No dyslipidemia	6 (3.1%)
BMI (kg/m²), median (range)	27.7 (16.8–41.6)
BMI category, n (%)	
Underweight (<18.5)	3 (1.5%)
Normal (18.5–22.9)	23 (11.8%)
Overweight (23–24.9)	26 (13.3%)
Obese class I (25–29.9)	98 (50.3%)
Obese class II (≥30)	45 (23.1%)
Systolic BP (mmHg), mean (SD)	138.7 (22.0)
Diastolic BP (mmHg), median (range)	84 (63–136)
HbA1c (%), median (range)	6.8 (4.7–13.9)
Fasting glucose (mg/dL), median (range)	121 (72–457)
2-hour postprandial glucose (mg/dL), median (range)	165 (71–567)
LDL (mg/dL), mean (SD)	133.4 (30.1)
Triglycerides (mg/dL), median (range)	137 (41–966)
HDL (mg/dL), median (range)	48 (2–104)
Total cholesterol (mg/dL), median (range)	214 (14–358)
eGFR (mL/min/1.73 m²), mean (SD)	75.9 (19.8)
ACR (mg/g), median (range)	29.9 (0.5–3662)
Albuminuria grade, n (%)	
Normal	98 (50.3%)
Microalbuminuria	75 (38.5%)
Macroalbuminuria	22 (11.3%)
ACR by albuminuria grade (mg/g), median (range)	
Normal	13.67 (0.5–29.9)
Microalbuminuria	85.87 (30.7–296.9)
Macroalbuminuria	954.71 (395.9–3662.3)
CIMT (mm), median (range)	0.76 (0.40–1.60)
CIMT by age group (mm), median (range)	
31–40 years	0.68 (0.48–1.01)
41–50 years	0.66 (0.42–1.19)
51–60 years	0.80 (0.40–1.42)
61–70 years	0.76 (0.45–1.45)
71–80 years	0.86 (0.69–1.60)

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Table 1: Continued.

Variable	Total (n=195)
CIMT status, n (%)	
Normal	118 (60.5%)
Increased	77 (39.5%)

in Table 2, median CIMT values increased progressively across albuminuria categories, from 0.73 mm in the normoalbuminuria group to 0.77 mm in the microalbuminuria group, and 0.84 mm in the macroalbuminuria group. The analysis demonstrated a weak but statistically significant positive correlation between albuminuria grade and the logarithmic value of CIMT (r=0.142, p=0.047), suggesting that higher degrees of albuminuria are modestly associated with increased CIMT.

To assess whether the association between albuminuria grade and CIMT in type 2 diabetes mellitus (T2DM) patients was independent of potential confounders, a multivariate analysis was performed. Variables with a p-value<0.250 in the bivariate analysis were included in the multiple linear regression model (Table 3).

In the bivariate analysis, age was positively associated with CIMT (r=0.295; p<0.001). Patients with a history of hypertension had significantly higher CIMT values compared to those without hypertension (p<0.001), and CIMT values also differed significantly between those who received diabetes treatment and those who did not (p=0.014). In contrast, sex, smoking history, dyslipidemia, and BMI were not significantly associated with CIMT (p>0.05). Variables with p<0.250 were included in a multivariate multiple linear regression to identify independent predictors of CIMT in T2DM patients (Table 4).

Multivariate analysis using multiple linear regression examined the independent association of albuminuria grade with CIMT, adjusting for age, hypertension history, and diabetes treatment. The overall model was significant (ANOVA $F(4,190)=10.599$, $p<0.001$) with $R=0.427$, $R^2=0.182$, and adjusted $R^2=0.165$. Age ($\beta=0.198$, $p=0.004$) and hypertension history ($\beta=0.297$, $p<0.001$) were independent predictors of increased CIMT, whereas albuminuria grade and diabetes treatment showed no significant association. Based on the multiple linear regression analysis, the predictive regression equation for the logarithm of CIMT is expressed as follows:

$$Y = -0.782 + 0.006 \times \text{Age} + 0.005 \times \text{Albuminuria Grade} + 0.188 \times \text{Hypertension History} + 0.039 \times \text{Diabetes Treatment}$$

This equation quantifies the relationship between CIMT and the included variables, indicating that age and hypertension history contribute positively to CIMT, while albuminuria grade and diabetes treatment show minimal impact in the adjusted model.

Ability of ACR in predicting increased CIMT in type 2 DM patients

The analysis revealed an area under the curve (AUC) of 0.489 (SE=0.044), with a non-significant p-value of 0.795, indicating no difference from the reference value of 0.5, which represents random discrimination. The 95% confidence interval ranged from 0.404 to 0.574, encompassing 0.5 and confirming the poor discriminatory ability of ACR in this study. Therefore, ACR is not a reliable standalone biomarker for distinguishing increased CIMT status in the studied population (Figure 1).

Table 2: Bivariate analysis of degree of albuminuria and CIMT.

Albuminuria grade	ACR (mg/g), median (range)	CIMT (mm), median (range)	Spearman correlation with log-CIMT
Normal	13.67 (0.5–29.9)	0.73 (0.40–1.31)	
Microalbuminuria	85.87 (30.7–296.9)	0.77 (0.42–1.60)	r=0.142*(p=0.047)
Macroalbuminuria	954.71 (395.9–3662.3)	0.84 (0.40–1.30)	

Note: Spearman correlation was used to test the association between albuminuria grade and log-transformed CIMT values. Statistically significant at α=0.05 (two-tailed test); n=195.

Table 3: Bivariate correlation of potential confounding variables with CIMT in T2DM patients.

Variable	CIMT (mm), median (range)	Correlation Coefficient (r)	P-value
Age	0.80 (0.40–1.60)	0.295	0.000 * [a]
Sex			
Male	0.75 (0.43–1.42)		0.781 [b]
Female	0.77 (0.40–1.60)		
Smoking history			
Current	0.78 (0.40–1.42)		
Former	0.74 (0.43–1.60)		0.610 [c]
Never	0.77 (0.42–1.45)		
Hypertension			
Yes	0.80 (0.42–1.60)		0.000 * [b]
No	0.59 (0.40–1.18)		
Dyslipidemia			
Yes	0.77 (0.40–1.60)		0.784 [b]
No	0.69 (0.57–0.98)		
Body Mass Index (BMI)	0.80 (0.40–1.60)	0.029	0.692 [d]
Diabetes treatment			
Yes	0.79 (0.42–1.45)		0.014 [b]
No	0.74 (0.40–1.60)		

Note: [a] – Pearson's correlation test; [b] – Independent t-test; [c] – One-way ANOVA; [d] – Spearman's correlation; * – Variables included in multivariate analysis.

Table 4: Multivariate multiple linear regression of predictors of CIMT in T2DM patients.

Variable	Unstandardized B	Std. Error	Standardized B	t	P-value	95% CI	Tolerance	VIF
Constant	-0.782	0.118		-6.649	<0.001	-1.014 to -0.550		
Age	0.006	0.002	0.198	2.879	0.004	0.002 to 0.010	0.907	1.103
Albuminuria grade	0.005	0.030	0.011	0.154	0.878	-0.054 to 0.064	0.813	1.230
Hypertension history	0.188	0.046	0.297	4.122	<0.001	0.098 to 0.278	0.827	1.208
Diabetes treatment	0.039	0.040	0.068	0.965	0.336	-0.041 to 0.118	0.858	1.166

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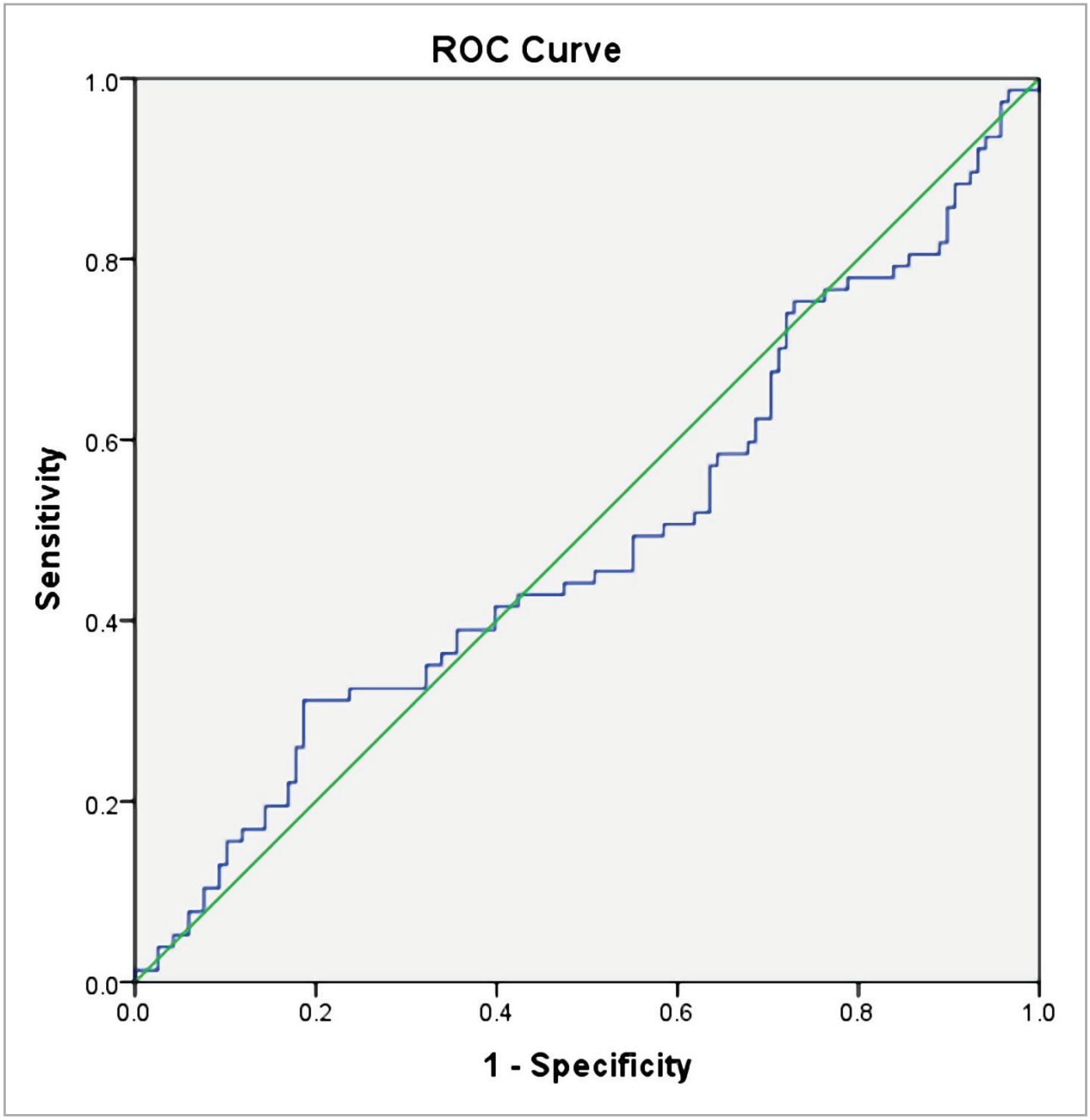

Figure 1: ROC curve.

Discussion

Albuminuria and carotid intima-media thickness (CIMT) are key indicators for evaluating microvascular and macrovascular complications in type 2 diabetes mellitus (T2DM). Albuminuria reflects glomerular damage, while increased CIMT indicates subclinical atherosclerosis and elevated cardiovascular risk. Both have been linked to higher morbidity and mortality in diabetic populations [13].

This study found a weak but significant positive correlation between albuminuria degree and CIMT in bivariate Spearman analysis (r=0.142; p=0.047), with median CIMT rising from 0.73 mm (normoalbuminuria) to 0.84 mm (macroalbuminuria). However, multivariate multiple linear regression analysis showed this association was not independent after adjusting for confounders such as age, hypertension, and diabetes therapy (p=0.878). Instead, hypertension history and age remained significant independent predictors of increased CIMT.

These findings align with previous studies reporting that although albuminuria correlates with early macrovascular changes, its predictive value diminishes

when major vascular risk factors are accounted for. Albuminuria represents systemic endothelial dysfunction caused by oxidative stress and chronic inflammation; mechanisms also implicated in atherosclerosis development. Yet, atherosclerosis is multifactorial; aging and hypertension exert strong effects on vascular remodeling and CIMT progression. Hypertension contributes to vascular wall thickening and endothelial injury, overshadowing albuminuria's impact on CIMT.14-16.

Moreover, the wide variability in albuminuria levels and complex interactions among risk factors in T2DM complicate the independent predictive role of albuminuria. Although biologically relevant, albuminuria alone is insufficient to predict subclinical atherosclerosis progression. These results emphasize the need for a multidimensional cardiovascular risk assessment in T2DM, integrating renal biomarkers, blood pressure, lipid profile, and age, rather than relying solely on albuminuria.

The Receiver Operating Characteristic (ROC) curve is a statistical method used to evaluate the performance of a biomarker in distinguishing between two conditions—in this case, increased carotid intima-media thickness (CIMT) status based on urinary albumin-to-creatinine ratio (ACR) in type 2 diabetes mellitus (T2DM) patients. ACR, as an indicator of early kidney damage, has potential associations with vascular changes, including CIMT progression.

The ROC analysis yielded an Area Under the Curve (AUC) of 0.489 (p=0.795; 95% CI: 0.404–0.574), indicating a very low discriminative ability of ACR to distinguish increased CIMT. The AUC below 0.5 and a non-significant p-value confirm that ACR cannot reliably differentiate patients with elevated CIMT in this population. Thus, ACR alone is an insufficient biomarker for predicting or identifying subclinical atherosclerosis in T2DM.

These ROC findings align with prior bivariate and multivariate analyses showing that although albuminuria correlates with CIMT, it is not an independent predictor after adjusting for confounders. This underscores that while albuminuria reflects endothelial dysfunction biologically, it is not a primary determinant of subclinical atherosclerotic changes measured by CIMT. Comprehensive cardiovascular risk assessment in T2DM should therefore incorporate multiple factors such as age, blood pressure, lipid profile, and glycemic control for more accurate prediction [13–17].

For clinical practice in primary care, regular assessment of the albumin-to-creatinine ratio (ACR) remains essential for early detection of renal complications in type 2 diabetes patients. However, evaluation of subclinical atherosclerosis risk should prioritize carotid intima-media thickness (CIMT) measurement, especially in older patients and those with a history of hypertension, as these factors have a greater influence on CIMT progression. For screening program development, it is recommended to implement a comprehensive vascular risk assessment combining multiple parameters—ACR, blood pressure, age, and lipid profile—to enhance early atherosclerosis detection in the diabetic population. Future research should adopt a longitudinal design to establish causal relationships between albuminuria and CIMT progression over time, incorporating additional measures such as inflammatory markers (*e.g.*, hs-CRP), hypertension duration, and detailed evaluation of antihypertensive and lipid-lowering therapies.

This study has several limitations. Firstly, the cross-sectional design precludes establishing causal relationships between albuminuria and carotid intima-media thickness (CIMT), restricting the findings to associative observations. Secondly, key confounding variables, including duration of hypertension, use of non-statin lipid-lowering therapies, types of antidiabetic medications, and history of alcohol consumption, were not examined, potentially influencing the progression of atherosclerosis. Thirdly, the gender distribution was markedly imbalanced, with a predominance of female participants (76.4%), which may introduce gender-related bias given the physiological differences in CIMT between sexes. Lastly, the wide variability in albumin-to-creatinine ratio (ACR) values (0.5–3,662 mg/g) may have contributed to statistical outliers and increased error, particularly affecting the discriminatory power observed in the ROC analysis, where the area under the curve (AUC) approached 0.5.

Conclusion

This study demonstrated a weak positive association between albuminuria and carotid intima–media thickness (CIMT) in individuals with type 2 diabetes mellitus (T2DM). However, after adjustment for major confounding factors, particularly age and hypertension, albuminuria was not independently associated with increased CIMT. These findings suggest that albumin-to-creatinine ratio (ACR) alone is not a reliable marker for identifying subclinical atherosclerosis when assessed using CIMT in a community-based T2DM population.

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The lack of an independent association indicates that macrovascular changes reflected by CIMT may be more strongly influenced by traditional cardiovascular risk factors rather than microvascular damage represented by albuminuria. Age-related vascular remodeling and hypertension appear to play a more dominant role in the development of early atherosclerosis. Therefore, comprehensive cardiovascular risk assessment in patients with T2DM should prioritize established risk factors in addition to microvascular markers.

Further longitudinal studies with larger sample sizes and repeated measurements of albuminuria and CIMT are warranted to clarify temporal relationships and potential causal pathways. Incorporating other markers of vascular dysfunction may also improve the early detection of atherosclerosis in T2DM, particularly in community-based settings.

Conflict of interest

The authors declare that we have no conflicts of interest related to this study. There were no financial or non-financial relationships that could be perceived to influence the conduct, analysis, or reporting of the research findings.

Ethics approval

This study was conducted using data from a previously approved protocol: Evaluation of Chronic Complications of Type 2 Diabetes Mellitus: PTM Bogor Cohort Follow-Up Study 2019–2020. The protocol was reviewed and approved by the Institutional Review Board (IRB)/Ethics Committee of the Faculty of Medicine, Universitas Indonesia (Approval No: KET-14/UN2.F1/ETIK/PPM.00.02/2019). All procedures were performed in compliance with the Declaration of Helsinki and the International Council for Harmonisation–Good Clinical Practice (ICH-GCP) guidelines.

Consent to participate

Written informed consent was obtained from all participants prior to enrollment in the study. All participants received a clear explanation regarding the study objectives, procedures, potential risks, and benefits, and participation was entirely voluntary in accordance with ethical research standards.

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