ORIGINAL RESEARCH / ORİJİNAL ARAŞTIRMA

DOI: 10.4274/kvbulten.galenos.2026.96268
Bull Cardiovasc Acad 2026;4(1):29-36

Association of Oscillometrically Estimated Cardiac Index With Microalbuminuria in Non-diabetic Adults With Preserved Kidney Function

Böbrek Fonksiyonu Korunmuş Non-diyabetik Erişkinlerde Osilometrik Olarak Tahmin Edilen Kardiyak İndeksin Mikroalbüminüri ile İlişkisi

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Abstract

Objectives: Microalbuminuria is a predictor of cardiovascular events even in non-diabetic individuals. Whether oscillometrically measured cardiac index (CI) is associated with early renal microvascular damage independently of metabolic risk and conventional blood pressure indices has not been systematically evaluated.In this study, we aimed to investigate the association of CI with the urinary albumin-to-creatinine ratio (UACR) in non-diabetic adults with preserved kidney function.

Material and Methods: A total of 99 non-diabetic adults with preserved kidney function were included in the study. Participants underwent oscillometric analysis, spot UACR measurement and biochemical assessment. The triglyceride-glucose (TyG) index was used as a marker of insulin resistance. Hierarchical linear regression models for log(UACR) were constructed by sequentially adding age and body mass index, the TyG index, and CI. Alternative hemodynamic parameters and multivariable logistic regression analyses for microalbuminuria were also evaluated.

Results: Median UACR was 9.92 mg/g (interquartile range 5.14-22.95), and the prevalence of microalbuminuria was 21.2%. Among all hemodynamic parameters, CI showed the strongest univariate correlation with log(UACR) ($r=0.505$, $p<0.001$). Adding CI to the metabolic base model increased the explained variance from 34.2% to 44.3% ($\Delta R^2 =0.101$; partial $F=14.90$; $p<0.001$). CI was independently associated with log(UACR) ($\beta=0.700$; 95% confidence interval 0.339-1.060; $p<0.001$) and remained significant after adjustment for sex, hypertension, smoking and resting heart rate.In comparative models, CI explained more residual variance in log(UACR) than any pressure-based hemodynamic index; moreover, brachial systolic blood pressure was not significant when entered into the same model as CI. The prevalence of microalbuminuria increased across CI quartiles, rising from 7.1% in Q1 to 50.0% in Q4 ($\chi^2=17.58$; $p<0.001$). In the parsimonious logistic model, both the TyG index and CI were independently associated with microalbuminuria.

Conclusion: In non-diabetic adults with preserved kidney function, CI was independently associated with renal microvascular damage in continuous-outcome analyses and explained variation in log(UACR) better than pressure-based hemodynamic indices in this cohort. Together with the independent contribution of the TyG index, these findings support a dual-pathway framework involving both metabolic and volumetric hemodynamic factors in subclinical nephropathy.

Keywords: Cardiac index, microalbuminuria, insulin resistance, triglyceride-glucose index, pulse wave analysis, renal hemodynamics

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Received/Geliş Tarihi: 17.04.2026 **Accepted/Kabul Tarihi:** 26.04.2026 **Published Date/Yayınlanma Tarihi:** 30.04.2026

Cite this article as/Atıf: Eşki S, Eravcı Ö, Taşkan H, Çakal S. Association of oscillometrically estimated cardiac index with microalbuminuria in non-diabetic adults with preserved kidney function. Bull Cardiovasc Acad. 2026;4(1):29-36

Öz

Amaç: Mikroalbüminüri, diyabetik olmayan bireylerde dahi kardiyovasküler olayların öngördürücüsüdür. Osilometrik ölçülen kardiyak indeksin (Kİ) metabolik risk ve konvansiyonel kan basıncı indekslerinden bağımsız olarak erken renal mikrovasküler hasar ile ilişkili olup olmadığı sistematik olarak değerlendirilmemiştir. Bu çalışmada, böbrek fonksiyonu korunmuş non-diyabetik erişkinlerde Kİ'nin idrar albümin/kreatinin oranı (UACR) ile ilişkisini araştırmayı amaçladık.

Yöntem ve Gereçler: Çalışmaya böbrek fonksiyonu korunmuş 99 non-diyabetik erişkin dahil edildi. Katılımcılara osilometrik nabız dalga analizi, spot UACR ölçümü ve biyokimyasal değerlendirme yapıldı. İnsülin direncinin göstergesi olarak trigliserid-glukoz (TyG) indeksi kullanıldı. Log(UACR) için oluşturulan hiyerarşik lineer regresyon modellerine sırasıyla yaş ve vücut kitle indeksi, TyG indeksi ve Kİ eklendi. Alternatif hemodinamik parametreler ile mikroalbüminüri (UACR ≥30mg/g) için çok değişkenli lojistik regresyon analizleri değerlendirildi.

Bulgular: Medyan UACR 9,92 mg/g (çeyrekler arası aralık 5,14-22,95) idi ve mikroalbüminüri prevalansı %21,2 olarak bulundu. Tüm hemodinamik parametreler arasında Kİ, log(UACR) ile en güçlü tek değişkenli korelasyonu gösterdi (r=0,505; p<0,001). Kİ'nin metabolik temel modele eklenmesi, açıklanan varyansı %34,2'den %44,3'e yükseltti (ΔR^2=0,101; kısmi F=14,90; p<0,001). Kİ, log(UACR) ile bağımsız olarak ilişkiliydi (β=0,700; %95 GA 0,339-1,060; p< 0,001) ve cinsiyet, hipertansiyon, sigara kullanımı ve dinlenim kalp hızı için düzeltmelerden sonra da anlamlılığını korudu. Karşılaştırmalı modellerde Kİ, log(UACR)'deki artık varyansı basınç temelli hemodinamik indekslerin tümünden daha fazla açıkladı; ayrıca brakiyal sistolik kan basıncı, Kİ ile aynı modele alındığında anlamlı değildi. Mikroalbüminüri prevalansı Kİ çeyrekleri boyunca arttı ve Q1'de %7,1'den Q4'te %50,0'ye yükseldi (χ^2=17,58; p<0,001). Kısıtlı lojistik modelde hem TyG indeksi hem de Kİ mikroalbüminüri ile bağımsız olarak ilişkili bulundu.

Sonuç: Böbrek fonksiyonu korunmuş non-diyabetik erişkinlerde, osilometrik olarak hesaplanan Kİ sürekli sonlanım analizlerinde erken renal mikrovasküler hasar ile bağımsız olarak ilişkili bulundu ve bu kohortta log(UACR)'deki varyasyonu basınç temelli hemodinamik indekslerden daha iyi açıkladı. TyG indeksinin bağımsız katkısıyla birlikte bu bulgular, subklinik nefropatide metabolik ve volümetrik hemodinamik faktörleri içeren ikili bir yolak çerçevesini desteklemektedir.

Anahtar Kelimeler: Kardiyak indeks, mikroalbüminüri, insülin direnci, trigliserid-glukoz indeksi, nabız dalga analizi, renal hemodinami

INTRODUCTION

Microalbuminuria, defined as a urinary albumin-to-creatinine ratio (UACR) of 30-300 mg/g, is an established biomarker of early renal microvascular damage and an independent predictor of cardiovascular morbidity and mortality, including in non-diabetic individuals without overt chronic kidney disease (CKD) (1-3). In this population, subclinical elevations in albuminuria reflect generalized endothelial dysfunction and increased glomerular capillary permeability, making the identification of modifiable determinants clinically important for early risk stratification.

Two principal pathways are implicated in early renal microvascular injury: metabolic and hemodynamic. On the metabolic side, insulin resistance conveniently estimated by the triglyceride-glucose (TyG) index has been linked to incident CKD and albuminuria through endothelial dysfunction, oxidative stress, and pro-fibrotic signaling (4,5). On the hemodynamic side, the kidney receives 20-25% of cardiac output through a high-flow, low-resistance vascular bed, rendering it sensitive to both pressure- and flow-mediated stress (6,7). To date, the hemodynamic component of renal risk has been studied predominantly through blood pressure and arterial stiffness indices (8,9). However, blood pressure is the product of cardiac output and systemic vascular resistance (SVR); the flow-mediated component, which directly augments renal perfusion, intraglomerular pressure, and ultrafiltration is not captured by pressure measurements alone and may contribute to glomerular hyperfiltration even when blood pressure is normal (10,11).

The cardiac index (CI), defined as cardiac output normalized to body surface area (BSA), aims to capture this flow-mediated component. Oscillometric pulse wave analysis provides non-invasive estimates of CI alongside conventional central and peripheral hemodynamic parameters (12), yet whether oscillometrically estimated CI is independently associated with early renal microvascular damage in non-diabetic adults has not been systematically evaluated. In the present cross-sectional study of non-diabetic adults with preserved kidney function, we examined the independent and incremental association between CI and log-transformed UACR after adjustment for age, body mass index (BMI), and the TyG index and compared CI with pressure-based hemodynamic indices. We hypothesized that CI would be independently associated with early renal microvascular damage in this population.

MATERIAL AND METHODS

This was a multicenter, cross-sectional observational study. To ensure inter-center consistency, all measurements were obtained by operators who had received standardized training on the Mobil-O-Graph 24h PWA Monitor. Consecutive adult patients (≥18 years) who underwent oscillometric pulse wave analysis,

spot UACR measurement, and standard laboratory assessment were screened for eligibility. The study protocol was approved by the Ethics Committee of Sivas Cumhuriyet University (approval no: 2026-02/11, date: 26.02.2026), and institutional permissions were obtained from participating centers as required. Written informed consent was obtained from all participants prior to enrollment.

A total of 147 patients were initially assessed for eligibility. The following exclusion criteria were applied: (i) diabetes mellitus, defined as fasting plasma glucose ≥126 mg/dL on two occasions, glycated hemoglobin ≥6.5%, or use of antidiabetic medication (n=21); (ii) impaired kidney function, defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² (n=3); and (iii) absence of spot urine UACR measurement (n=24), as the primary outcome variable required documented urinary albumin excretion. After these exclusions, 99 non-diabetic individuals with preserved kidney function and available UACR data constituted the final analytic cohort.

Demographic and clinical data were obtained from medical records. Recorded variables included age, sex, BMI (kg/m²), BSA (m²), smoking status (current smoker vs. non-smoker), and comorbidities, including hypertension, coronary artery disease, hyperlipidemia, and chronic obstructive pulmonary disease. Antihypertensive treatment status (yes/no), number of antihypertensive drug classes, and regimen composition were documented.

Venous blood samples were obtained after an overnight fast of at least 8 hours. Standard biochemical parameters included fasting plasma glucose, serum creatinine, uric acid, complete blood count, and lipid profile (total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides). The eGFR was calculated using the CKD epidemiology collaboration equation.

The TyG index, a surrogate marker of insulin resistance, was calculated using the formula: TyG index=ln [triglycerides (mg/dL)×fasting plasma glucose (mg/dL)/2]. This index has been validated as a reliable surrogate for insulin resistance and correlates strongly with the hyperinsulinemic-euglycemic clamp technique.

A spot midstream urine sample, preferably collected in the early morning, was obtained from each participant to determine urinary microalbumin (mg/L) and urinary creatinine (mg/L). The UACR was calculated as [urinary microalbumin concentration (mg/L)/urinary creatinine concentration (mg/L)]×1000 and expressed in mg/g. Microalbuminuria was defined as UACR ≥30 mg/g in accordance with KDIGO guidelines.

For regression analyses, UACR was natural log-transformed [log(UACR)] to approximate a normal distribution and to linearize its relationship with predictor variables. Log(UACR) served as the primary continuous-outcome, while the binary classification of microalbuminuria (UACR ≥30 mg/g) served as the secondary categorical outcome.

Brachial blood pressure was measured with the participant seated after at least 5 minutes' rest, using an appropriately sized cuff on the non-dominant arm. Systolic (bSBP) and diastolic (bDBP) blood pressures were recorded. Mean arterial pressure was calculated as bDBP+(bSBP-bDBP)/3. Resting heart rate was recorded simultaneously. Brachial hemodynamic data were available for all 99 participants.

Central hemodynamic parameters were assessed non-invasively using an oscillometric pulse wave analysis device (Mobil-O-Graph 24h PWA Monitor; I.E.M. GmbH, Stolberg, Germany). This validated device reconstructs the central aortic pressure waveform from brachial oscillometric recordings using a generalized transfer function and provides the following parameters: central SBP, central DBP, central pulse pressure, augmentation pressure, augmentation index corrected to 75 beats per minute (AIx@75), and aortic pulse wave velocity (PWV). Additionally, the device estimates cardiac output, stroke volume (SV), SVR, and cardiac index. The cardiac index, defined as cardiac output normalized to BSA (L/min/m²), was the primary hemodynamic exposure variable, as it represents the volumetric flow load delivered to the renal microvasculature per unit body size.

All measurements were performed by trained operators at each center according to a standardized study protocol in a quiet, temperature-controlled room with the patient in a seated position after at least 10 minutes' rest. At least two consecutive recordings were obtained, and the mean values were used for analysis.

Statistical Analysis

Continuous variables were tested for normality using the Shapiro-Wilk test and are presented as mean ± standard deviation or median [interquartile range (IQR)], as appropriate; categorical variables are presented as frequencies and percentages. The primary outcome was log(UACR) as a continuous variable, with cardiac index as the main hemodynamic exposure. Categorical microalbuminuria (UACR ≥30 mg/g) analyses were considered secondary because of the limited number of events. Univariate associations with log(UACR) were assessed using Spearman's rank correlation coefficients. Hierarchical linear regression was performed by sequentially adding age and BMI, the TyG index, and the cardiac index. The incremental value of cardiac index was evaluated using ΔR^2, the partial F-test, the likelihood ratio test, and the AIC. Alternative hemodynamic parameters were entered separately in place of cardiac index. Participants

were also stratified by cardiac index quartiles. Between-group comparisons were assessed using ANOVA or the Kruskal-Wallis test; trend was assessed by Spearman correlation; and microalbuminuria prevalence was assessed by the chi-square test. Multivariable logistic regression was performed with microalbuminuria as the outcome variable. Sensitivity analyses were performed by adding each variable separately: brachial SBP, antihypertensive treatment, sex, hypertension, smoking, and resting heart rate. Model assumptions were assessed using variance inflation factors (VIF), the Durbin-Watson statistic, the Breusch-Pagan test, and the Shapiro-Wilk test of residuals; HC3 robust standard errors were used where appropriate. Missing data were handled by complete-case analysis. All analyses were performed using IBM SPSS Statistics version 26.0 and Python 3.12 (pandas, SciPy, statsmodels). A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Of the 147 patients initially assessed, 48 were excluded (21 with diabetes mellitus, 3 with eGFR <60 mL/min/1.73 m², and 24 with missing UACR), yielding a final cohort of 99 non-diabetic individuals with preserved kidney function. The cohort was predominantly female (66.7%), with a median age of 54 years (IQR 49-61); hypertension and current smoking were each present in 48.5% of participants. Median UACR was 9.92 mg/g (IQR 5.14-22.95), and microalbuminuria (UACR ≥30 mg/g) was detected in 21 participants (21.2%). The mean TyG index was 8.77±0.56 (available in 87 participants), and median cardiac index was 2.60 L/min/m² (IQR 2.40-3.00). Full baseline characteristics are shown in Table 1.

In univariate Spearman correlation analysis, cardiac index showed the strongest correlation with log(UACR) among all variables examined (r=0.505, p<0.001), followed by SV (r=0.459), triglycerides (r=0.435), the TyG index (r=0.386), central SBP (r=0.383, n=84), and cardiac output (r=0.300); brachial SBP was not significantly correlated (r=0.154, p=0.129). Cardiac index and the TyG index were virtually uncorrelated (r=0.056, p=0.581), consistent with independent hemodynamic and metabolic contributions.

Hierarchical linear regression for log(UACR) is shown in Table 2 (n=87). Age and BMI together explained 11.7% of the variance; adding the TyG index raised R^2 to 0.342 (ΔR^2=0.225, p<0.001); adding cardiac index raised R^2 further to 0.443 (ΔR^2=0.101; partial F=14.90, p<0.001; likelihood ratio χ^2=14.52, p<0.001; ΔAIC=12.5). Cardiac index was independently associated with log(UACR) (β=0.700, 95% CI 0.339-1.060, p<0.001), corresponding to a 0.70-unit increase in log(UACR) per 1 L/min/m² increase in cardiac index. Standardized coefficients indicated that the TyG index had the largest effect (βstd=0.469), followed by the cardiac index (0.334) and BMI (-0.310).

When cardiac index was replaced by each alternative hemodynamic parameter in Model 3 (Table 3), cardiac index provided the largest incremental contribution (ΔR^2=0.101), followed by SV (0.091), cardiac output (0.063), and SVR (0.046); brachial SBP (ΔR^2=0.006, p=0.396) and PWV (ΔR^2=0.000) did not contribute significantly. When cardiac index and brachial SBP were entered together, cardiac index remained significant (β=0.792, p<0.001) and brachial SBP did not (β=-0.006, p=0.332). In smaller subsamples with available data, central SBP (ΔR^2=0.114, n=72) and AIx@75 (ΔR^2=0.021, n=84) were also evaluated.

Table 1. Baseline clinical, metabolic, and hemodynamic characteristics (n=99)

Variable	Value	Variable	Value
Age, years	54.0 (49.0-61.0)	Serum creatinine, mg/dL	0.75 (0.68-0.89)
BMI, kg/m²	29.5 (26.6-33.1)	eGFR, mL/min/1.73 m²	93.0 (83.0-103.0)
Female sex, n (%)	66 (66.7)	UACR, mg/g	9.92 (5.14-22.95)
Hypertension, n (%)	48 (48.5)	Microalbuminuria, n (%)	21 (21.2)
Current smoking, n (%)	48 (48.5)	Brachial SBP, mmHg	134.0 (123.0-148.0)
Fasting glucose, mg/dL	90.0 (82.0-99.0)	Brachial DBP, mmHg	88.0±15.1
Triglycerides, mg/dL†	127.0 (106.0-227.0)	Heart rate, bpm	76.0 (70.0-83.0)
HDL cholesterol, mg/dL†	47.0 (40.0-54.0)	Cardiac index, L/min/m²	2.60 (2.40-3.00)
LDL cholesterol, mg/dL†	116.0 (104.0-134.0)	Cardiac output, L/min	5.00 (4.50-5.70)
TyG index†	8.77±0.56	Stroke volume, mL	65.1 (58.4-70.7)
SVR, s·mmHg/mL	1.30 (1.20-1.50)	PWV, m/s	8.00 (7.60-8.90)
Central SBP, mmHg‡	132.0 (123.8-145.8)	AIx@75, %§	30.5 (17.3-36.3)

Note: Data are mean ± standard deviation or median (interquartile range); categorical variables n (%)
†: Available in n=87; ‡: n=84, §: n=96, TyG: Triglyceride-glucose, SVR: Systemic vascular resistance, PWV: Pulse wave velocity, AIx@75: Augmentation index at 75 bpm, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, UACR: Urinary albumin-to-creatinine ratio, BMI: Body mass index

Across cardiac index quartiles (≤2.4, 2.5-2.7, 2.8-3.0, >3.0 L/min/m²; n=99; Table 4), mean log(UACR) increased monotonically from 1.91±0.94 in Q1 to 3.37±0.77 in Q4 (ANOVA F=13.97, p<0.001; Spearman p-for-trend: r=0.505, p<0.001), and microalbuminuria prevalence rose from 7.1% in Q1 to 50.0% in Q4 (χ^2=17.58, p<0.001).

In the parsimonious logistic regression model (n=87, 21 events, events-per-variable=10.5), both the TyG index [odds ratio (OR) 3.53, 95% CI 1.21-10.35, p=0.021] and cardiac index (OR 3.63, 95% CI 1.28-10.25, p=0.015) were independently associated with microalbuminuria; adding cardiac index to a TyG-only model significantly improved fit (likelihood ratio χ^2=6.44, p=0.011). In a sensitivity analysis with additional adjustment for age and BMI (events-per-variable=5.2), TyG remained significant (OR 7.72, p=0.001), whereas the association of cardiac index attenuated and became non-significant (OR 2.25, p=0.134), consistent with reduced statistical power.

Model 3 diagnostics showed no problematic multicollinearity (all VIF ≤1.25). The Breusch-Pagan test indicated heteroscedasticity (p<0.001); however, HC3 standard errors confirmed the significance of all conclusions (cardiac index: HC3 p=0.005; TyG: p<0.001). Residuals showed a mild departure from normality (Shapiro-Wilk W=0.932, p<0.001), which did not affect the substantive conclusions given the sample size.

Cardiac index remained independently associated with log(UACR) in every sensitivity model tested (Table 5). Adjustment for brachial SBP, antihypertensive treatment, sex, hypertension, current smoking, or resting heart rate did not attenuate the association. A single model including all four additional covariates together yielded β=0.834 (95% CI 0.388-1.280, p<0.001). Of the added covariates, only resting heart rate reached statistical significance in its respective model (β=-0.024 per bpm, p=0.015).

Table 2. Hierarchical linear regression models for log(UACR) (n=87)

Variable	β (SE)	95% CI	p	βstd	R^2 (Adj)
Model 1: Age + BMI					
Age	0.025 (0.011)	0.004 to 0.047	0.021	0.227	
BMI	-0.050 (0.021)	-0.093 to -0.008	0.020	-0.242	0.117 (0.096)
Model 2: + TyG index					
Age	0.015 (0.010)	-0.004 to 0.034	0.119	0.143	
BMI	-0.086 (0.020)	-0.126 to -0.047	<0.001	-0.417	
TyG index	0.968 (0.182)	0.607 to 1.329	<0.001	0.515	0.342 (0.318)
Model 3: + cardiac index					
Age	0.017 (0.009)	0.000 to 0.035	0.054	0.165	
BMI	-0.064 (0.019)	-0.102 to -0.026	0.001	-0.310	
TyG index	0.881 (0.169)	0.544 to 1.219	<0.001	0.469	
Cardiac index	0.700 (0.181)	0.339 to 1.060	<0.001	0.334	0.443 (0.416)

Note: Incremental values: Adding TyG index to Model 1, ΔR^2=0.225, p<0.001. Adding cardiac index to Model 2, ΔR^2=0.101 (partial F=14.90, p<0.001; likelihood ratio χ^2=14.52, p<0.001; ΔAIC=12.5). ΔR^2 indicates the additional variance explained by the variable. A lower AIC denotes a better model fit
β: Unstandardized coefficient, SE: Standard error, CI: Confidence interval, βstd: Standardized coefficient, BMI: Body mass index, TyG: Triglyceride-glucose, UACR: Urinary albumin-to-creatinine ratio

Table 3. Comparative hemodynamic models for log(UACR): contribution beyond the metabolic base model (n=87)

Parameter	β	p	R^2	ΔR^2
Cardiac index	0.700	<0.001	0.443	0.101
Stroke volume	0.029	<0.001	0.432	0.091
Cardiac output	0.338	0.004	0.405	0.063
SVR	-1.071	0.015	0.388	0.046
Brachial SBP	0.005	0.396	0.348	0.006
PWV	0.030	0.844	0.342	0.000

Note: Each model adjusts for age, BMI, and the TyG index; cardiac index is substituted with each alternative parameter. ΔR^2=change in R^2 compared with the metabolic base model. Central SBP (ΔR^2=0.114, n=72) and AIx@75 (ΔR^2=0.021, n=84) were analyzed in smaller subsamples due to missing data and are reported in-text only
BMI: Body mass index, TyG: Triglyceride-glucose, SVR: Systemic vascular resistance, SBP: Systolic blood pressure, AIx@75: Augmentation index at 75 bpm, PWV: Pulse wave velocity, UACR: Urinary albumin-to-creatinine ratio

Table 4. Log(UACR) and microalbuminuria prevalence across cardiac index quartiles (n=99)

Quartile	CI (L/min/m²)	n	Log(UACR), mean ± SD	Microalbuminuria n/N	Prevalence %
Q1	≤2.4	42	1.914±0.939	3/42	7.1
Q2	2.5-2.7	21	2.287±1.124	3/21	14.3
Q3	2.8-3.0	12	2.544±0.709	3/12	25.0
Q4	>3.0	24	3.371±0.765	12/24	50.0

Note: ANOVA: F=13.970, p<0.001; Kruskal-Wallis: H=34.594, p<0.001; p-for-trend (Spearman): r=0.505, p<0.001; χ^2 for microalbuminuria: 17.581, p<0.001
ANOVA: Analysis of Variance, UACR: Urinary albumin-to-creatinine ratio, SD: Standard deviation, CI: Cardiac index

Table 5. Sensitivity analyses: cardiac index coefficient after additional adjustment (Model 3 base: age, BMI, TyG index, cardiac index; n=87)

Additional covariate	CI β	95% CI	CI p	Covariate p
Brachial SBP	0.792	-	<0.001	0.332
Antihypertensive treatment	0.693	-	<0.001	0.734
Sex (female)	0.639	0.275 to 1.003	<0.001	0.098
Hypertension status	0.700	0.337 to 1.063	<0.001	0.934
Current smoking	0.586	0.188 to 0.985	0.004	0.194
Resting heart rate	0.925	0.531 to 1.318	<0.001	0.015
All four simultaneously†	0.834	0.388 to 1.280	<0.001	-

†: Model including sex, hypertension, smoking, and heart rate together, alongside age, BMI, and TyG index, SBP: Systolic blood pressure, CI: Confidence interval, BMI: Body mass index, TyG: Triglyceride-glucose

DISCUSSION

In this cross-sectional study of 99 non-diabetic individuals with preserved kidney function, the cardiac index showed an independent association with early renal microvascular damage, as assessed by the log-transformed UACR. Among the hemodynamic parameters examined, cardiac index showed the largest univariate correlation with log(UACR) and accounted for the largest share of the residual variance in multivariable models. The association was independent of age, BMI, and metabolic risk represented by the TyG index, and adding cardiac index to the metabolic base model increased the explained variance from 34.2% to 44.3% (ΔR^2=0.101, p<0.001). A monotonic gradient was observed across cardiac index quartiles, with the prevalence of microalbuminuria rising from 7.1% in Q1 to 50.0% in Q4. In the parsimonious logistic model, both TyG index and cardiac index were independently associated with microalbuminuria; however, in the fully adjusted logistic model, the association of cardiac index with categorical microalbuminuria was attenuated to non-significance (OR 2.25, p=0.134). We interpret this attenuation as potentially related to limited statistical power (events-per-variable= 5.2; only 21 events), although we cannot entirely exclude the possibility that the independent association may be genuinely weaker when UACR is evaluated as a categorical outcome.

Among the hemodynamic parameters examined, cardiac index, an oscillometric estimate of volumetric flow normalized to BSA, explained the largest additional share of variance in log(UACR) (ΔR^2=0.101), while brachial SBP contributed negligibly (ΔR^2=0.006, p=0.396). When both were included, cardiac index remained statistically significant (p<0.001), while brachial SBP was not statistically significant (p=0.332). Notably, adjusting for resting heart rate did not attenuate the association between cardiac index and log(UACR); if anything, the coefficient for cardiac index increased (β=0.925, p<0.001), suggesting that the observed association was not simply driven by chronotropic effects embedded in the oscillometric estimate of SV and cardiac output. These observations are descriptive and based on a single cohort; whether cardiac index has comparable explanatory value in other populations remains to be determined.

This observation is physiologically plausible. Blood pressure is a composite variable reflecting the product of cardiac output and SVR. Two individuals may share identical brachial SBP values yet differ in their hemodynamic phenotype: one with high cardiac output and low resistance (hyperdynamic circulation), the other with low output and high resistance (13). In hyperdynamic states, increased renal blood flow has been associated with elevated intraglomerular pressure and shear stress, mechanisms thought to contribute to glomerular hyperfiltration and endothelial injury (14,15). This pathway is well-described in obesity, where

elevated cardiac output is associated with renal hyperfiltration that can precede overt albuminuria (16,17). Our findings suggest that this flow-mediated pathway may also operate in a broader non-diabetic population and can be approximated non-invasively through oscillometric hemodynamic phenotyping. Causal inference is not possible from the present cross-sectional design.

The TyG index was the strongest overall correlate of log(UACR) (standardized β=0.469), consistent with the established role of insulin resistance in renal microvascular injury even at normal fasting glucose (4,18). Cardiac index and the TyG index were virtually uncorrelated (r=0.056, VIF=1.00), suggesting that the hemodynamic and metabolic pathways operate largely through independent mechanisms. This dual-pathway framework—metabolic dysfunction and volumetric hemodynamic load—offers a parsimonious model for early renal microvascular damage in non-diabetic individuals, although confirmation in longitudinal studies is required. The inverse association between BMI and log(UACR) observed after adjustment for the TyG index might hypothetically reflect a statistical suppression effect: once the TyG index absorbs the metabolic risk associated with adiposity, the residual BMI term may capture non-metabolic components of body composition or a dilutional effect on urinary albumin concentration (19). This interpretation is post hoc and should be regarded as exploratory.

A monotonic gradient in microalbuminuria prevalence was observed across cardiac index quartiles, rising from 7.1% in the lowest quartile to 50.0% in the highest. The CAFE and Strong Heart studies showed superior prognostic performance of central over brachial blood pressure for cardiovascular events (20,21), but did not examine cardiac output-based parameters; cardiac output has been linked to renal function decline in heart failure (22), and altered renal hemodynamics have been described in obesity (17). The present study extends these observations to a general non-diabetic ambulatory population. Oscillometric hemodynamic phenotyping is widely available and may yield information complementary to conventional blood pressure measurement; however, the cross-sectional nature of the present data does not justify routine clinical use of the oscillometric cardiac index for renal risk stratification. The findings should be confirmed in prospective, multicenter cohorts.

Study Limitations

This study has several limitations. First, the cross-sectional design precludes causal inference; whether elevated cardiac index precedes or simply co-occurs with microalbuminuria cannot be determined from the present data. Second, statistical power is constrained. The multivariable analytic sample size was n=87, and there were only 21 microalbuminuria events. The fully adjusted logistic model (events-per-variable=5.2) should be regarded as hypothesis-generating; even the parsimonious model yields wide confidence intervals. The discordance between the strong continuous-outcome association and the attenuated full-model categorical association likely reflects low statistical power rather than a genuine difference. In addition, microalbuminuria was defined using a single spot UACR measurement. Third, although the primary models adjusted for age, BMI, the TyG index, brachial SBP, and antihypertensive treatment, residual confounding cannot be excluded. Dietary sodium intake, physical activity, and Homeostatic Model Assessment for Insulin Resistance were not available. Finally, the cardiac index was estimated using oscillometric pulse wave analysis. Importantly, this is a mathematical estimate rather than a direct measurement using reference-standard methods.

CONCLUSION

In non-diabetic adults with preserved kidney function, oscillometrically estimated cardiac index was independently associated with early renal microvascular damage in analyses of continuous outcomes and explained a larger share of the variance in log(UACR) than did pressure-based hemodynamic indices. The association was robust across multiple sensitivity analyses, including adjustment for sex, hypertension, smoking, antihypertensive treatment, and resting heart rate. When combined with the strong and independent contribution of the TyG index, these findings are consistent with a dual-pathway framework in which metabolic dysfunction and volumetric hemodynamic load are jointly associated with subclinical nephropathy through complementary mechanisms. Given the cross-sectional design, the limited number of microalbuminuria events, the use of a single spot UACR measurement, and the surrogate nature of oscillometrically estimated cardiac index, the present results should be regarded as hypothesis-generating. Prospective studies with repeated UACR measurements, larger samples, and reference-standard hemodynamic assessment are warranted before any clinical application can be considered.

*Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Sivas Cumhuriyet University (approval no: 2026-02/11, date: 26.02.2026), and institutional permissions were obtained from participating centers where required. All procedures were performed in accordance with the ethical standards of the responsible ethics committee, the participating institutions, and the 1964 Declaration of Helsinki and its later amendments.

Informed Consent: Written informed consent was obtained from all participants prior to enrollment.

Footnotes

Data Availability

The de-identified dataset analyzed during the current study is available from the corresponding author upon reasonable request.

Authorship Contributions

Surgical and Medical Practices: S.E., Ö.E., Concept: S.E., Ö.E., H.T., S.Ç., Design: S.E., Ö.E., H.T., S.Ç., Data Collection or Processing: S.E., Ö.E., Analysis or Interpretation: S.E., Ö.E., H.T., S.Ç., Literature Search: S.E., Ö.E., H.T., Writing: S.E., Ö.E., H.T., S.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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