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Autonomic and Inflammatory Markers Associated with Reduced Glomerular Filtration Rate in Non-Dialysis Chronic Kidney Disease: A Cross-Sectional Study

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Abstract

Background: Chronic kidney disease (CKD) progression is influenced by metabolic comorbidities such as diabetes and hypertension and is frequently accompanied by impaired cardiovascular autonomic regulation. Although autonomic imbalance and systemic inflammation are both linked to adverse renal outcomes, their combined contribution to variability in estimated glomerular filtration rate (eGFR) in non-dialysis CKD patients remains unclear. This study aimed to evaluate whether autonomic function parameters and inflammatory markers are associated with eGFR beyond traditional clinical predictors.

Methods: This cross-sectional study included 43 patients with chronic kidney disease not receiving dialysis. Clinical data were obtained from medical records. Fasting blood samples were collected for creatinine, cystatin C, urea, and interleukin-6 measurements. eGFR was calculated using the combined creatinine–cystatin C equation. Heart rate variability (HRV) was recorded using a validated smartphone application and analyzed with Kubios HRV Scientific software. Blood pressure was measured with a digital sphygmomanometer.

Results: Interleukin-6 showed a significant negative correlation with eGFR. In contrast, most HRV parameters were not individually correlated with renal function. Multiple linear regression analysis explained 44.1% of the variance in eGFR. Although RMSSD (a parasympathetic index) alone did not independently predict eGFR after adjustment, the final multivariable model identified RMSSD, serum urea, and interleukin-6 as significant predictors alongside conventional variables such as body mass index and sex. **Conclusion:** Parasympathetic modulation (RMSSD) and systemic inflammation (interleukin-6) are independently associated with renal function in non-dialysis CKD patients, suggesting that combining heart rate variability and inflammatory markers may improve clinical assessment and early risk stratification.

Keywords: autonomic dysfunction; glomerular filtration rate; chronic kidney disease; kidney-heart axis.

1. Introduction

Chronic kidney disease (CKD) is characterized by the persistent loss of kidney function and is widely recognized as a major global public health concern [1]. Approximately 10% of the adult population worldwide is affected by some stage of CKD, and cardiovascular disease remains the leading cause of mortality in this population [2]. In Brazil, although the true prevalence of CKD is still uncertain, survey-based estimates suggest that about 1.5% of individuals self-report kidney disease [3].

According to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines, CKD is defined by abnormalities in kidney structure or function, or a glomerular filtration rate (GFR) below 60 ml/min/1.73 m^2, persisting for at least three months and associated with adverse health outcomes [4]. CKD progression is multifactorial and involves genetic susceptibility as well as common metabolic disorders, particularly type 2 diabetes mellitus and arterial hypertension [1].

The estimated glomerular filtration rate (eGFR), the primary clinical indicator of renal function, may be influenced by several factors including age, sex, albuminuria, and the underlying disease [5]. Importantly, cardiovascular conditions such as heart failure have been linked to accelerated declines in eGFR [6]. This reflects the well-established bidirectional interaction between the heart and kidneys, in which dysfunction in one organ promotes injury in the other through mechanisms involving systemic inflammation, neurohormonal activation, and oxidative stress—processes collectively described as cardiorenal syndrome [7-8].

Within this framework, patients with CKD frequently exhibit impaired cardiovascular autonomic regulation, typically characterized by sympathetic

overactivity and reduced parasympathetic modulation [9]. Although both autonomic dysfunction and chronic low-grade inflammation are individually recognized as contributors to cardiovascular and renal complications in CKD, their combined clinical relevance as indicators of impaired renal function remains insufficiently understood. In particular, studies that simultaneously examine cardiac autonomic parameters and inflammatory biomarkers in relation to estimated glomerular filtration rate (eGFR) among non-dialysis CKD patients are scarce, limiting opportunities for earlier clinical risk stratification.

Therefore, the present study aimed to investigate cross-sectional associations among cardiac autonomic function parameters, inflammatory biomarkers, and eGFR to identify clinically relevant indicators of reduced renal function in non-dialysis patients with chronic kidney disease.

2. Methods

Study design and participants

This cross-sectional study was conducted at the nephrology outpatient clinic of the Lauro Wanderley University Hospital, in Brazil, between March and December 2025. The protocol was approved by the institutional ethics committee (CAAE 83625324900005183), and all participants provided written informed consent before enrollment. Eligible participants were adults (>18 years) diagnosed with chronic kidney disease (CKD) stages G2–G4 (pre-dialysis), with an estimated glomerular filtration rate (eGFR) between 15 and 89 ml/min/1.73 m². CKD stages were classified according to the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines using eGFR thresholds, with stages defined as G2 (60–89 ml/min/1.73 m²), G3a (45–59 ml/min/1.73 m²), G3b (30–44 ml/min/1.73 m²), and G4 (15–29 ml/min/1.73 m²).

Exclusion criteria included CKD secondary to autoimmune diseases, history of kidney transplantation, single kidney, polycystic kidney disease or other structural nephropathies, human immunodeficiency virus infection, liver disease, pregnancy, and use of supplements such as probiotics, prebiotics, synbiotics, or antioxidant compounds.

A total of 53 patients were initially recruited through simple random sampling in January–February 2025. Ten participants were excluded for not meeting eligibility criteria (liver disease n=4; autoimmune CKD n=3; kidney transplantation n=2; single kidney n=1), resulting in a final sample of 43 participants. Given the exploratory nature and limited sample size, hierarchical modeling was used to minimize overfitting, and results should be interpreted as hypothesis-generating.

Clinical and anthropometric assessment

Demographic and clinical characteristics, including age, sex, and medication use, were obtained from structured questionnaires and confirmed through medical records. Body weight and height were measured using a calibrated digital scale with an attached stadiometer, and body mass index (BMI) was calculated as weight divided by height squared (kg/m²). Nutritional status was classified according to WHO criteria for adults [10] and Lipschitz criteria [11] for older individuals.

Blood collection and biochemical measurements

Fasting blood samples (8–12 h) were collected at the hospital by trained nursing staff. Approximately 10 mL of blood was obtained and distributed into separator gel tubes and EDTA tubes. After centrifugation (10 min, 3,500 rpm), serum aliquots were stored at −80 °C until analysis.

Serum creatinine was measured using an enzymatic method (Labtest®, ref. 127), and urea was determined by a colorimetric enzymatic assay (Labtest®, ref. 27). Cystatin C was measured by immunoturbidimetry using a Labmax 240 analyzer with Turbiquest Plus reagent (Labtest®, ref. 350). Interleukin-6 concentrations were quantified by enzyme-linked immunosorbent assay using a commercial high-sensitivity kit and read on a Synergy LX multidetection microplate reader.

The glomerular filtration rate was estimated using the combined creatinine–cystatin C CKD-EPI equation and normalized to body surface area using standard height and weight adjustments [12].

Blood pressure and heart rate variability assessment

Resting blood pressure (BP) and heart rate were measured in a controlled environment (24 ± 2 °C; relative humidity 50 ± 10%). The participants abstained from caffeinated or stimulant beverages for 24 h before BP and electrocardiogram (ECG) recording. Participants remained seated and measurements were obtained after at least 3 minutes of rest using a validated digital sphygmomanometer, following current Brazilian Guidelines of Hypertension [13].

Heart rate variability (HRV) was recorded during the afternoon (2:00 – 4:00 p.m) for 15 minutes in the supine position. RR intervals were captured using a chest strap heart rate transmitter (Polar H10) connected wirelessly to a smartphone application. This method has been previously validated for beat-to-beat recording [14,15]. RR interval files were exported and analyzed using Kubios HRV Scientific software (version 4.1.2). Kubios automatic artifact correction was applied.

The following HRV indices were evaluated: Time domain: root mean square of successive differences (RMSSD); Frequency domain: low frequency (LF), high frequency (HF), and LF/HF ratio; Nonlinear analysis: Poincaré plot indices SD1 and SD2 [16].

Statistical analysis

Descriptive statistics were calculated as mean ± standard deviation or relative frequencies, as appropriate. Associations between variables were assessed using Pearson correlation coefficients and multiple linear regression models. Predictor variables included age, body mass index, systolic blood

pressure, cardiac autonomic parameters, and inflammatory markers, with eGFR defined as the dependent variable. Variables were selected based on clinical relevance rather than automated selection. All analyses were performed using SPSS for Windows (version 21.0, IBM Corp.). Statistical significance was set at $p \leq 0.05$ with a 95% confidence interval.

Results

The clinical characteristics of the participants are presented in **Table 1**. The sample included 43 individuals, of whom 55.8% were women. The majority of participants were in advanced CKD stages, with distribution as follows: G2 (n = 2), G3a (n = 5), G3b (n = 23), and G4 (n = 13). Arterial hypertension was the most prevalent noncommunicable chronic disease (88.4%), followed by diabetes mellitus (51.2%), which showed a similar distribution between sexes. Nearly half of the participants (46.5%) reported engaging in regular physical activity. The most frequently used medications were hypoglycemic agents (62.8%), lipid-lowering agents (58.1%), and angiotensin II receptor blockers (44.2%).

Clinical, biochemical, hemodynamic, and cardiac autonomic parameters are summarized in **Table 2**. Participants had a mean age of 66.7 ± 12.4 years and a mean body mass index of 28.1 ± 5.2 kg/m². The mean estimated glomerular filtration rate (eGFR) was 34.6 ± 13.6 ml/min/1.73 m². Mean serum creatinine, cystatin C, and urea concentrations were 1.93 ± 0.44 mg/dL, 2.05 ± 0.99 mg/L, and 68.92 ± 11.63 mg/dL, respectively. Interleukin-6 concentrations were elevated in both men (10.00 ± 3.18 pg/mL) and women (8.68 ± 3.23 pg/mL). Systolic blood pressure values were elevated in both sexes and were higher among men (158.6 ± 31.7 mmHg). Mean heart rate variability indices were also numerically higher in men.

Correlation analyses are shown in **Table 3**. Estimated glomerular filtration rate was positively correlated with anthropometric parameters including body weight, waist circumference, and body mass index, as well as with serum urea. In contrast, interleukin-6 showed a strong negative correlation with eGFR. Heart rate variability indices were not significantly correlated with eGFR. Power LF

showed positive correlations with anthropometric parameters, while serum urea was negatively correlated with RMSSD.

Multiple linear regression models predicting eGFR are presented in **Table 4**. All hierarchical models reached statistical significance. The fully adjusted model, which included demographic, anthropometric, cardiac autonomic, and biochemical variables, explained 44.1% of the variance in eGFR (adjusted R^2 = 0.441, $p < 0.001$). In this final model, RMSSD, serum urea, and interleukin-6 were independently associated with eGFR, in addition to sex and body mass index, which remained significant predictors across models. The unexpected direction between RMSSA and eGRF should be interpreted cautiously and may reflect medication use, sample size, or residual confounding.

Discussion

The main findings of this study show that parasympathetic modulation (RMSSD), serum urea, and interleukin-6 were independently associated with renal function in non-dialysis chronic kidney disease, jointly explaining 44.1% of the variability in eGFR. Few studies have jointly evaluated vagally mediated HRV indices and inflammatory biomarkers as combined correlates of renal function in non-dialysis CKD, and our results indicate that lower vagal activity, greater uremic burden, and increased systemic inflammation are linked to reduced kidney function.

Hierarchical modeling further demonstrated that autonomic indices alone were not independently associated with eGFR; however, after inclusion of biochemical markers, RMSSD emerged as a significant predictor together with urea and IL-6, markedly improving model performance. This pattern suggests that autonomic dysfunction and inflammatory burden may interact and provide complementary clinical information beyond traditional demographic predictors.

Previous studies have examined the relationship between heart rate variability and CKD, although some did not use eGFR as the primary outcome [17,18] or emphasized frequency-domain parameters as more relevant [19][20]. RMSSD is strongly influenced by parasympathetic nervous system activity and represents the principal time-domain measure used to estimate vagally mediated modulation of heart rate [20]. In non-dialysis CKD patients, Drawz et al. demonstrated that RMSSD was associated with CKD outcomes and mortality, supporting its role as a prognostic autonomic marker [21]. Our findings reinforce the potential relevance of vagally mediated HRV indices in renal dysfunction.

Some studies with larger CKD cohorts have reported significant correlations between HRV parameters and eGFR [9, 22], including positive associations with RMSSD and negative associations with LF/HF ratio [9]. Reduced RMSSD has also been linked to lower renal function [21]. However, in our study, HRV parameters were not significantly correlated with eGFR in univariate analyses, consistent with findings from Chandra et al. [17], Costa et al. [23], and large cohort studies such as CRIC [21] and PREVEND [18]. Differences between studies may reflect variation in sample size, CKD stage distribution, comorbidity burden, and methodological approaches.

Autonomic abnormalities are known to increase with CKD progression [24]. Although CKD patients typically present reduced RMSSD [21] and increased LF/HF ratio [18], our HRV values were comparable to those reported in control populations in some studies [9] despite a mean eGFR corresponding to stage G3 CKD. One explanation may be the widespread use of medications affecting autonomic regulation. Beta-blockers, for example, reduce sympathetic activity and may modify HRV indices, and their use has been associated with altered RMSSD values [21]. Additionally, differences in HRV acquisition protocols, including recording duration, device type, and analysis approach may contribute to heterogeneous findings across studies [21, 24, 25, 26].

The pathophysiological mechanisms linking autonomic dysfunction and CKD outcomes remain incompletely understood. Autonomic imbalance is considered a complication of renal injury [27] characterized by sympathetic overactivity and reduced parasympathetic tone [28]. Chronic inflammation and uremic toxicity may further affect cardiac innervation and autonomic centers in the brainstem and peripheral ganglia [9, 29], supporting the biological plausibility

of associations between inflammatory markers, HRV alterations, and renal impairment.

Consistent with this framework, our study identified serum urea as an independent predictor of eGFR. Elevated urea levels are expected in CKD because of reduced renal excretion[33] and may rise markedly as disease progresses [30-32]. Previous studies have also demonstrated associations between urea or blood urea nitrogen levels and declining renal function [31-32]. Moreover, increased urea concentrations have been linked to cardiovascular risk [31] and systemic inflammation through mechanisms including intestinal barrier disruption [33]. These findings support the relevance of uremic burden as both a marker of renal impairment and a contributor to cardiovascular risk in CKD [34].

In addition, we observed a strong inverse association between IL-6 and eGFR, consistent with previous reports [35, 36]. IL-6 is a central inflammatory cytokine involved in immune activation [37-39] and has been associated with mortality risk in CKD [40-42], as well as cardiovascular events [42]. Increased IL-6 levels in CKD may result from oxidative stress, persistent inflammation, and reduced cytokine clearance [37]. Together, these mechanisms reinforce the contribution of inflammation to cardiorenal interactions and renal function decline.

Anthropometric parameters such as BMI, waist circumference, and body weight showed positive correlations with eGFR in our sample. Although this contrasts with some previous reports, differences in CKD stage distribution and the use of the CKD-EPI creatinine–cystatin C equation, which adjusts for body surface area, may partially explain this observation. Associations between waist circumference and frequency-domain HRV indices observed in our study are consistent with prior investigations linking central adiposity to autonomic

modulation [32]. Obesity-related hyperfiltration has been proposed as an early renal phenotype that may precede functional decline [43].

This study has several strengths, including detailed medication assessment, comprehensive HRV evaluation across time, frequency, and nonlinear domains, and the integration of inflammatory and biochemical markers in hierarchical regression models. However, limitations should be acknowledged. The relatively small sample size may limit statistical power and generalizability. In addition, the cross-sectional design precludes causal inference. Although the HRV acquisition method was validated and conducted under standardized conditions, device-based recordings may differ from conventional electrocardiographic monitoring. Future longitudinal and multicenter studies with larger samples are needed to clarify the prognostic role of HRV indices and inflammatory markers in CKD progression and to determine whether targeting autonomic dysfunction may improve renal outcomes.

Conclusion

In this study, renal function was independently associated with autonomic, inflammatory, and metabolic markers when evaluated jointly. RMSSD was the only cardiovascular autonomic index retained in the adjusted model, together with BMI, sex, serum urea, and interleukin-6, indicating that parasympathetic modulation, uremic burden, and systemic inflammation contribute to renal impairment in CKD. Although RMSSD was not predictive alone, its significance after adjustment highlights the importance of integrated cardiorenal and inflammatory assessment.

Overall, higher IL-6 and urea levels, along with altered RMSSD, were associated with lower eGFR and may help improve risk stratification in CKD. These findings support the interaction between autonomic dysfunction, inflammation, and kidney function, and suggest that HRV assessment may provide a complementary clinical value in the monitoring of patients with CKD, particularly in those with cardiorenal risk.

Ethics approval and consent to participate

Federal University of Paraiba Review Committee approved this study (number 83625324900005183). This study was conducted in accordance with the Declaration of Helsinki

Consent for publication

Not applicable

Clinical trial number

Not applicable

Competing interests

The authors declare that they have no competing interests

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Author contributions

PMPL: Conception and study design, data collection and analysis, writing the manuscript first draft, and revising and editing. ACS: Conception and study design, revising and editing the manuscript, and supervision. EMAB, AISL and RSS: data collection and analysis and revise the manuscript. VJBM: data analysis and revising the manuscript for intellectual content. JLBA: Conception and study

design, revising the manuscript, project administration, and supervision. All authors have approved the final manuscript.

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Availability of data and materials

The datasets used and/ or analyzed during this study are available from the corresponding author on reasonable request.

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Table 1. Clinical characteristics, comorbidities, medication use, and lifestyle factors of the study participants

Variables	Man (n=19; 44.2%)	Woman (n=24; 55.8%)	Total (n=43)
Noncommunicable Diseases			
Diabetes Mellitus n (%)	11 (50.0)	11 (50.0)	22 (51.2)
Hypertension n (%)	17 (45.0)	21 (55.0)	38 (88.4)
Dyslipidemia n (%)	1 (8.3)	11 (91.7)	12 (27.9)
Cardiovascular Disease n (%)	6 (7.5)	10 (62.5)	16 (37.2)
Current Medications			
Angiotensin II blockers n (%)	10 (52.63)	9 (47.37)	19 (44.2)
Diuretics n (%)	9 (50.0)	9 (50.0)	18 (41.9)
Beta-blockers n (%)	5 (29.41)	12 (70.59)	17 (39.5)
Lipid-lowering agents	11 (44.0)	14 (56.0)	25 (58.1)
Hypoglycemic agents	10 (37.04)	17 (62.96)	27 (62.8)
Calcium channel blockers n (%)	8 (57.14)	6 (42.8)	14 (32.6)
Vasodilators n (%)	11 (73.33)	4 (26.67)	15 (34.9)
Angiotensin-converting enzyme inhibitors n (%)	3 (30.0)	7 (70.0)	10 (23.3)
Practice of physical activity	9 (45.0)	11 (55.0)	20 (46.5)

Values are presented as number (%). Distribution is shown according to sex and for the total sample (n = 43). Noncommunicable diseases include diabetes mellitus, hypertension, dyslipidemia, and cardiovascular disease. Medication classes correspond to current treatments recorded at the time of clinical evaluation

Table 2. Clinical, biochemical, hemodynamic, and cardiac autonomic parameters of participants

Variables	Man (n=19) Mean (min-max)	SD	Woman (n=24) Mean (min-max)	SD	Total (n=43) Mean	SD
Age (Years)	68.75 (47.98-93.73)	12.69	65.14 (43.20-84.96)	12.20	66.73	12.40
BMI (kg/m²)	28.64 (19.33-38.23)	4.90	27.84 (15.16-42.82)	5.59	28.19	5.25
eGFR (ml/min/1.73 m²)	39.16 (18-80)	17.07	31.00 (15-56)	9.12	34.60	13.68
Creatinine (mg/dL)	1.92 (1.20-3.43)	0.49	1.95 (1.30-2.97)	0.41	1.93	0.44
Cystatin C (mg/L)	2.25 (0.80-4.90)	1.13	1.90 (1.00-4.30)	0.86	2.05	0.99
Urea (mg/dL)	67.42 (41.00-87.40)	10.78	70.11 (51.60-101.30)	12.36	68.92	11.63
IL6 (pg/mL)	10.00 (5.10-15.40)	3.18	8.68 (4.20-16.70)	3.23	9.26	3.23
SBP (mmHg)	158.58 (82-224)	31.67	142.79 (95-185)	19.74	149.77	26.57
RMSSD (ms)	32.66 (2.5-108.2)	26.97	39.37 (6.3-73.6)	18.74	36.41	22.70
Power LF (%)	47.93 (10.66-72.97)	15.12	43.38 (14.46-66.80)	14.09	45.39	14.56
LF/HF ratio	1.82 (0.12-4.39)	1.22	1.22 (0.17-4.60)	1.01	1.48	1.13
SD2/SD1	1.99 (0.94-4.15)	0.86	1.63 (0.72-2.80)	0.56	1.79	0.72

Continuous variables are expressed as mean (minimum–maximum) and standard deviation (SD), stratified by sex and for the total sample (n = 43). Abbreviations: BMI = body mass index; eGFR = estimated glomerular filtration rate; IL-6 = interleukin-6; SBP = systolic blood pressure; RMSSD = root mean square of successive differences; LF = low frequency; HF = high frequency.

Table 3. Pearson correlation coefficients between clinical, biochemical, and autonomic variables and estimated glomerular filtration rate

	eGFR	SBP	DBP	Waist	Weight	BMI	RMSSD	Power LF	LH/HF	SD2/SD1	IL-6
SBP	0.073										
DBP	-0.060	0.491**									
Waist	0.381**	0.124	-0.305*								
Weight	0.447**	0.047	-0.248*	0.790**							
BMI	0.279*	0.109	-0.277*	0.825**	0.832**						
RMSSD	-0.193	-0.137	-0.181	0.120	0.092	0.104					
Power LF	-0.028	0.016	-0.276*	0.316*	0.299*	0.315**	0.292*				
LF/HF	0.013	0.341**	-0.077	0.210	0.191	0.191	-0.340**	-0.791**			
SD2/SD1	-0.085	0.181	-0.026	0.223	0.144	0.139	-0.050	0.449**	0.574**		
IL-6	-0.313**	-0.046	-0.039	-0.073	0.145	-0.041	0.219	-0.060	-0.050	0.050	
Urea	0.359**	0.093	-0.014	-0.250*	-0.134	-0.043	-0.286*	0.043	-0.090	-0.079	-0.009

Correlation coefficients (r) were calculated using Pearson's test. Abbreviations: eGFR = estimated glomerular filtration rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index. Values were significantly different: *p<0.05, **p<0.01.

Table 4. Hierarchical multiple linear regression models predicting estimated glomerular filtration rate

Variables	B	SE for B	Beta Coefficient	*p*	*P* Value (ANOVA)	Adjusted R square
Model 1						
Constant	30.665	16.935		0.075		
Age	-0.045	0.124	-0.045	0.720		
Sex	-7.539	3.415	-0.278	0.031	0.040	0.102
BMI	0.615	0.273	0.267	0.028		
SBP	-0.014	0.063	-0.028	0.823		
Beta blockers	2.150	3.018	0.087	0.479		
Model 2						
Constant	42.787	17.617		0.018		
Age	0.115	0.132	0.114	0.388		
Sex	-7.728	3.327	-0.285	0.024		
BMI	0.924	0.285	0.401	0.002		
SBP	-0.078	0.071	-0.154	0.281		
Beta blockers	3.951	3.289	0.160	0.235	0.014	0.179
Power LF	-0.389	0.204	-0.453	0.062		
LF/HF Ratio	2.595	2.775	0.231	0.354		
SD2/SD1	-3.195	0.075	-0.239	0.231		
RMSSD	-0.138	0.075	-0.239	0.068		
Model 3						
Constant	80.171	16.190		0.000		
Age	-0.004	0.111	-0.004	0.971		
Sex	-7.792	2.879	-0.288	0.009		
BMI	0.813	0.236	0.353	0.001		
SBP	-0.010	0.062	-0.019	0.875		
Beta blockers	4.292	2.719	0.174	0.120	0.000	0.441
Power LF	-0.195	0.175	-0.227	0.269		
LF/HF Ratio	-0.677	2.431	-0.060	0.782		
SD2/SD1	-1.912	2.190	-0.104	0.386		
RMSSD	-0.168	0.067	-0.290	0.015		
Urea	-0.457	0.112	-0.439	0.000		
IL-6	-1.143	0.377	-0.300	0.004		

Multiple linear regression models were constructed hierarchically to evaluate predictors of estimated glomerular filtration rate (eGFR).
Model 1 included demographic and clinical variables.
Model 2 additionally included cardiac autonomic parameters.
Model 3 additionally included biochemical markers.
B = unstandardized coefficient; SE = standard error; β = standardized coefficient; Adjusted R^2 = adjusted coefficient of determination.
Sex coded as 1 = men and 2 = women; Beta-blocker use coded as 1 = yes and 2 = no.
Statistical significance is defined as $p < 0.05$.