

Microalbuminuria Predicts Elevated Right Ventricular Filling Pressure in Non-Obstructive Coronary Artery Disease

Mahdokht Rezaei¹, Elham Ebadi¹, Abbas Allami^{2*}, Kimia Rahimi Ardali³, Shahin Aliakbari³

Received: 27 Aug 2024

Published: 1 Jul 2025

Abstract

Background: While microalbuminuria is established in left heart dysfunction prognostication, its relationship with right ventricular (RV) function remains unclear. We investigated whether microalbuminuria predicts early-stage RV dysfunction in patients with normal coronary arteries.

Methods: This cross-sectional analysis involved 117 patients with angiography-verified non-obstructive CAD. Comprehensive RV echocardiography (including E/e' ratio) and morning urine albumin-creatinine ratio (UACR) measurements were performed. The study patients were categorized into 67 with normal albuminuria (mAlb (-): UACR <30 mg/g) and 50 with microalbuminuria (mAlb (+): UACR 30-300 mg/g). Multivariable logistic regression evaluated microalbuminuria's relationship with RV metrics, adjusting for sex, age, and BMI. A $P < 0.05$ denoted statistical significance.

Results: The mAlb (+) group demonstrated significantly higher RV E/e' ratios ($P = 0.026$), persisting after adjustment. Logistic regression revealed that microalbuminuria independently predicted elevated RV filling pressure (OR 2.88, 95% confidence interval 1.22-6.84, $P = 0.016$). Male sex showed non-significant trends (OR 1.69, $P = 0.286$). RV systolic dysfunction prevalence was comparable between groups (16.4% overall, $p = NS$).

Conclusion: Microalbuminuria independently associates with elevated RV filling pressures in non-obstructive CAD patients, suggesting shared microvascular pathophysiology. This supports albuminuria screening's potential role in identifying subclinical RV dysfunction, though longitudinal studies are needed to establish causality.

Keywords: Albuminuria, Right Ventricle, Coronary Vessels

Conflicts of Interest: None declared

Funding: None

*This work has been published under CC BY-NC-SA 4.0 license.

Copyright© Iran University of Medical Sciences

Cite this article as: Rezaei M, Ebadi E, Allami A, Rahimi Ardali K, Aliakbari S. Microalbuminuria Predicts Elevated Right Ventricular Filling Pressure in Non-Obstructive Coronary Artery Disease. *Med J Islam Repub Iran*. 2025 (1 Jul);39:88. <https://doi.org/10.47176/mjiri.39.88>

Introduction

Research has consistently demonstrated that individuals with cardiovascular and cerebrovascular diseases exhibiting low levels of microalbuminuria face an elevated risk of mortality. These findings highlight microalbuminuria, even at minimal levels, as a significant predictor of cerebrovascular and cardiovascular mortality (1). Furthermore,

increased microalbuminuria is associated with the progression of diabetes mellitus (DM), hypertension (HTN), and overall mortality related to these conditions (2-5). Reducing microalbuminuria has been associated with a decreased incidence of cardiovascular diseases, including heart failure (HF) (6, 7). Elevated urinary albumin excre-

Corresponding author: Dr Abbas Allami, allami@qums.ac.ir

1. Department of Cardiology, BouAli Hospital, Qazvin University of Medical Sciences, Qazvin, Iran

2. Department of Infectious Diseases, BouAli Hospital, Qazvin University of Medical Sciences, Qazvin, Iran

3. Research Committee, Qazvin University of Medical Sciences, Qazvin, Iran

↑What is “already known” in this topic:

Microalbuminuria is established as an early indicator of renal dysfunction and is linked to a higher likelihood of cardiovascular complications, especially in patients with diabetes and hypertension. Identifying microalbuminuria as a possible sign of RV dysfunction could assist in detecting individuals at increased risk of negative cardiovascular events, enabling earlier intervention strategies.

→What this article adds:

- First evidence that microalbuminuria independently predicts elevated RV filling pressure (OR 2.88) in non-obstructive CAD patients.
- Proposes microalbuminuria as a practical screening tool for subclinical RV dysfunction.

tion has also been identified as a predictor of cardiovascular disease mortality (8). A high prevalence of microalbuminuria in HF patients correlates with increased cardiovascular mortality and frequent hospitalizations due to HF, particularly when an elevated urinary albumin-to-creatinine ratio (UACR) is present (9). Additionally, microalbuminuria is linked to cardiovascular risk factors such as DM and HTN, serving as a predictive indicator for cardiovascular complications (10). Several studies underscore the prognostic significance of microalbuminuria in coronary artery disease (CAD) and HF patients (6, 9, 10). Here's a discussion section based on the findings from the study you provided: The study by Yurtdas et al. (2017) highlights a significant relationship between heart rate (HR) recovery and microalbuminuria in patients with non-obstructive CAD. This suggests that microalbuminuria may serve as an indicator of autonomic dysfunction in this patient population. Furthermore, the authors reported that patients with non-obstructive CAD and abnormal HR recovery exhibited elevated UACR levels. The notable inverse association between UACR and HR recovery, particularly in patients with microalbuminuria, underscores the potential of microalbuminuria as a predictor of cardiac autonomic imbalance (11).

Right-sided HF is linked with poor clinical outcomes in both acute and chronic HF, acute myocardial infarction, and congenital heart disease, regardless of the underlying mechanisms (12). It is also correlated with increased mortality in patients with HF, CAD, pulmonary hypertension, and valvular heart disease (13). Recent research has explored the potential relationship between microalbuminuria and increased left ventricular (LV) mass (14), however, the connection between microalbuminuria and right ventricular (RV) function remains poorly understood.

This study aimed to determine the association between microalbuminuria and early-stage RV dysfunction using echocardiography in individuals with normal coronary arteries. The study focuses on identifying subtle RV functional changes detectable by echocardiography in the presence of microalbuminuria, before the onset of overt right-sided HF, and in the absence of confounding CAD. This approach will help elucidate the mechanisms by which microalbuminuria may contribute to the initiation and development of early-stage right-sided HF.

Methods

Study design

This investigation employed a cross-sectional design to evaluate patients undergoing angiography at BouAli Sina Hospital (Qazvin) during the period from April 2019 through March 2020. Inclusion criteria comprised patients with normal or minimally affected coronary arteries (stenosis <50%) as determined by angiography, sinus rhythm on electrocardiogram (ECG), and a LV ejection fraction greater than 50% on echocardiography. Exclusion criteria included: unwillingness to cooperate (refusal to provide complete or accurate responses to study questions and assessments), history of radiofrequency ablation in the management of cardiac arrhythmias or cardiac surgery, congenital heart disease, cardiomyopathy, defibrillation or

cardiac arrest within the past three months, moderate to severe valvular insufficiency, pulmonary arterial pressure (PAP) exceeding 45 mmHg, renal or urinary disease, macroalbuminuria, creatinine levels above 1.5 mg/dl, uncontrolled or untreated thyroid disease, and liver enzymes greater than twice the normal limit. To assess the presence of urinary tract infections (UTIs) in patients, we evaluated patient-reported symptoms and conducted urinalysis, analyzing for leukocyte esterase, nitrites, and blood, which aids in excluding UTIs, particularly in those with transient microalbuminuria. Eligible subjects were selected after a thorough explanation of the study's purpose and obtaining informed written consent.

Data Collection

Basic demographic and clinical information were gathered through questionnaires and health screenings, including age, gender, body mass index (BMI), HR, systolic and diastolic blood pressure (BP), medical history (including DM and HTN), medications, family history of heart diseases, and smoking status. DM was defined as a previous diagnosis of the condition, along with the current use of any glucose-lowering medications and a random plasma glucose level of ≥ 200 mg/dL (15). HTN was defined as elevated BP ($\geq 140/90$ mmHg) or documented antihypertensive medication use for 6 months or longer (16). The Glomerular Filtration Rate (GFR) was estimated using the Modification of Diet in Renal Disease (MDRD) equation (17).

Early morning urine samples were obtained from all study patients, which were examined both manually and automatically using the dipstick method, followed by microscopic examination of the urine sediment. If urinalysis showed no hematuria or hemoglobin excretion, urinary albumin and creatinine levels were measured. Participants were stratified based on their urine albumin-to-creatinine ratio values: without microalbuminuria (mAlb (-): Alb/Cr <30 mg/g) and with microalbuminuria (mAlb (+): Alb/Cr = 30-300 mg/g) (2).

Echocardiography

Echocardiography was performed on all patients to assess RV systolic function. These patients were candidates for coronary angiography due to risk factors such as acute coronary syndromes, positive noninvasive cardiac tests, valvular heart disease, and structural heart disease. The echocardiography was conducted according to the 2011 AUC criteria (18). All echocardiographic assessments were performed using the Affinity 50 and 70 Philips Ultrasound Machines (Philips Healthcare, Andover, MA, USA) with the S5-1 probe. Measurements were taken in accordance with ASE guidelines, with averages calculated over three cardiac cycles. The evaluation of RV systolic function was conducted using three key methods: RV peak systolic myocardial velocity (RVSm), RV fractional area change (RVFAC), and tricuspid annular plane systolic excursion (TAPSE). TAPSE was assessed using the M-mode marker line in the apical four-chamber view, which measures the maximum systolic velocity of longitudinal annular motion. A TAPSE value greater than 17 mm indi-

cates normal RV function, while values below 17 mm suggest dysfunction. RVFAC quantifies the percentage change in RV surface area between the post-systolic and end-diastolic phases, with normal values exceeding 35% and abnormal values falling below this threshold. RVSm reflects the systolic velocity of RV myocardial tissue, with normal values defined as greater than 9.5 cm/s. Current right heart echocardiography guidelines mandate the systematic inclusion of quantitative RV functional parameters in clinical reporting, with a specific recommendation to incorporate at least one validated measure during routine examinations. This is particularly crucial when RV dysfunction is suspected or when the clinical indication for the study pertains to conditions that may affect the RV. In our study, RV systolic dysfunction is considered likely if two or more of these parameters are found to be abnormal (19). RV hemodynamics were assessed solely through the E/e' ratio as a measure of filling pressure, without comprehensive diastolic function grading (20).

Echocardiographic indicators of RV structure and function, such as RV end-diastolic and end-systolic area (adjusted for body size) (21). Echocardiograms were analyzed and interpreted by researchers who were unaware of the laboratory data, clinical outcomes, and study results. We calculated the RVFAC using the formula: $RVFAC = (RVEDA - RVESA) / RVEDA \times 100\%$, where RVEDA (cm²) represents the RV end-diastolic area, indicating the volume of blood in the ventricle before contraction, and RVESA (cm²) represents the RV end-systolic area, indicating the volume of blood remaining in the ventricle after contraction. Additionally, RV systolic motion (RVSm) measures the movement of the RV during systole and serves as an indicator of RV function. In this study, the

tricuspid valve E wave (early diastolic tricuspid inflow velocity) was assessed using pulsed-wave Doppler, with the sample volume positioned at the tips of the tricuspid valve leaflets in the apical four-chamber view during the early diastolic phase. The RV e' (early diastolic velocity derived from tissue Doppler) was evaluated at the lateral tricuspid annulus using tissue Doppler imaging.

Statistical Analysis

Continuous variables were presented as median (interquartile range) for non-normally distributed data (analyzed with the Mann-Whitney U test) or as mean \pm standard deviation for normally distributed data (analyzed with the independent t-test), with normality determined using the Kolmogorov-Smirnov test. Categorical variables were expressed as counts (%) and compared using the χ^2 test or Fisher's exact test. Binary logistic regression, adjusted for sex, age, and BMI, was used to assess microalbuminuria as a predictor of increased RV filling pressure, with the model restricted to four predictors to maintain statistical power due to sample size limitations. All statistical analyses were conducted using SPSS version 27 (IBM Corp.), with a *P*-value <0.05.

Results

Study Population Characteristics

The analysis included 117 participants after excluding three patients with macroalbuminuria, comprising 67 controls (non-microalbuminuria group) and 50 cases (microalbuminuria group). Both groups were age-matched (mAlb (-): 56 \pm 11 vs mAlb (+): 55 \pm 10 years). The microalbuminuria group showed significantly greater preva-

Table 1. Basic, demographic, medical, and paraclinical information of patients with and without microalbuminuria

Variable	mAlb (-) n=67	mAlb (+) n=50	<i>P</i> value
Age (year)	56 \pm 11	55 \pm 10	0.695
Gender			
Male	21 (31.3)	24 (48.0)	0.067
Female	46 (68.7)	26 (52.0)	
BMI (kg/m ²)	26.78 (25.05 - 29.42)	27.13 (24.50 - 29.26)	0.760
BSA (m ²)	1.84 \pm 0.13	1.86 \pm 0.11	0.289
Medical history			
Diabetes	8 (11.9)	14 (28.0)	0.028*
Family history of heart disease	11 (16.4)	5 (10.0)	0.318
Smoking	17 (25.4)	18 (36.0)	0.214
Hyperlipidemia	19 (28.4)	7 (14.0)	0.065
Hypertension	11 (16.4)	20 (40.0)	0.004*
Medication used			
Aspirin	15 (22.4)	7 (14.0)	0.251
Beta-blocker	4 (6.0)	7 (14.0)	0.141
ACEi/ARB	10 (14.9)	20 (40.0)	0.002*
Statin	20 (29.9)	8 (16.0)	0.082
Insulin	1 (1.5)	6 (12.0)	0.018*
Oral diabetes medications	7 (10.4)	8 (16.0)	0.374
Antidiabetic medications	8 (11.9)	14 (28.0)	0.028*
Clinical and paraclinical findings			
SBP (mmHg)	125 (115 - 135)	129.5 (115 - 140)	0.211
DBP (mmHg)	80 (70 - 80)	80 (70 - 90)	0.072
Blood sugar (mg/dl)	139 (120 - 165)	156 (127 - 205)	0.058
BUN (mg/dl)	15 (12 - 19)	18 (15 - 21)	0.003*
Cr (mg/dl)	0.9 (0.8 - 1.0)	1.0 (0.9 - 1.1)	0.006*
eGFR (mg/dl)	69.5 (60.0-79.1)	70.5 (55.5-77.9)	0.457
UACR (mg/g)	16.8 (13.2-23.5)	65.4 (48.4-124.3)	<0.001*

Abbreviations: BUN: blood urea nitrogen, Cr: creatinine, ACEi/ARB: angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers, BSA: body surface area, BMI: body mass index, DBP: diastolic blood pressure, SBP: systolic blood pressure, eGFR: Estimated Glomerular Filtration Rate, mAlb: microalbuminuria, LVEF: left ventricular ejection fraction, SD: standard deviation, UACR: Urine Albumin/Creatinine ratio

Table 2. Echocardiographic findings in patients with and without microalbuminuria

Variable	mAlb (-)	mAlb (+)	P value
Left cardiac echocardiography			
LA diameter (cm)	34 (32 - 36)	33 (32 - 36)	0.770
Septum Thickness (cm)	8 (8 - 9)	8 (8 - 9)	0.696
Post Wall Thickness (cm)	8 (8 - 9)	8 (8 - 9)	0.653
LVEF (%)	56 (55-60)	57 (55-60)	0.824
LVEDD (cm)	49 (45 - 51)	48 (46 - 51)	0.969
LVESD (cm)	27 (24 - 30)	27 (24 - 30)	0.971
LVEDV (mL)	65 (52 - 80)	70 (53 - 80)	0.352
LVESV (mL)	27 (20 - 33)	29 (22 - 34)	0.288
LA Volume (mL)	46 (36 - 58)	38 (32 - 51)	0.064
Mitral E Velocity (m/s)	1 (1 - 1)	1 (1 - 1)	0.656
Mitral A Velocity (m/s)	1 (1 - 1)	1 (1 - 1)	0.075
Mitral DT (ms)	211 (169 - 257)	204 (169 - 232)	0.411
E' Septum (cm/s)	7 (6 - 9)	7 (6 - 8)	0.534
Septum A' (cm/s)	8 (7 - 9)	8 (7 - 9)	0.748
Lateral E' (cm/s)	10 (8 - 12)	9 (7 - 12)	0.643
Lateral A' (cm/s)	9 (7 - 11)	10 (7 - 11)	0.349
Right cardiac echocardiography			
RV systolic dysfunction	11 (16.4)	7 (14)	0.720
TAPSE (mm)	20 (18 - 22)	20 (18 - 22)	0.822
RVSm (cm/s)	11 (11 - 13)	11 (11 - 12)	0.757
RVFAC (%)	56 (48 - 62)	54.5 (46 - 60)	0.448
RV e' (cm/s)	4.71 (3.91 - 6.13)	5.36 (4.16 - 6.64)	0.076
RV - E/e' ratio	<6 >6	31 (62.0) 19 (38.0)	0.026*
E/A ratio	1.01 (0.90 - 1.20)	1.02 (0.88 - 1.14)	0.871
DT (ms)	275 (239 - 327)	262 (222 - 317)	0.396
RVEDA (cm ²)	24.63 19.63 28.27	26.42 (21.24 - 30.19)	0.174
RVESA (cm ²)	12.71 ± 4.12	13.16 ± 4.14	0.565
RVEDD (mm)	28 (25 - 30)	29 (26 - 31)	0.174
RAVI (mL/m ²)	19.60 (18.01 - 23.29)	19.42 (18.50 - 22.70)	0.993
TRV (m/s)	2.2 (2.1 - 2.4)	2.3 (2.1 - 2.4)	0.192
TRG (mmHg)	19 (17 - 24)	22 (19 - 24)	0.112
sPAP (mmHg)	22 (20 - 27)	25 (22 - 27)	0.112

Abbreviations: A: Peak velocity in late diastole, DT: deceleration time, E: peak velocity in early diastole, E': early diastolic tricuspid annular tissue peak velocity, RAVI: right atrial volume index, RV: right ventricle, RVEDD: right ventricle end-diastolic diameter, RVEDA: Right Ventricular End-Diastolic Area, RVESA: Right Ventricular End-Systolic Area, RVFAC: RV fractional area change, RVSM: right ventricular peak systolic myocardial velocity, sPAP: Systolic pulmonary artery pressure, TAPSE: tricuspid Annular Plane Systolic Excursion, TRG: tricuspid regurgitant jet gradient, TRV: tricuspid regurgitant jet velocity

lence of DM ($P=0.028$) and HTN ($P=0.004$), along with elevated renal markers (BUN: $P=0.003$; Cr: $P=0.006$) compared to controls. Complete demographic and clinical characteristics are presented in Table 1.

RV systolic dysfunction was identified in 11 patients (16.4%), with comparable prevalence between groups ($P>0.05$). While UACR levels were numerically higher in patients with RV systolic dysfunction (57.75 ± 51.9 vs 49.92 ± 44.26 mg/g), this difference did not reach statistical significance. Notably, the mAlb (+) group demonstrated significantly impaired RV diastolic function, evidenced by elevated RV E/e' ratios ($P=0.026$). Complete hemodynamic comparisons are presented in Table 2.

After controlling for sex, age, and BMI, microalbuminuria emerged as a significant independent predictor of elevated RV filling pressure (adjusted OR 2.88, 95% CI 1.22-6.84, $P=0.016$). The model demonstrated non-significant trends for male sex (OR 1.69, 95% CI 0.65-4.43, $P=0.286$), while neither age (OR 1.01 per year, 95% CI 0.97-1.06) nor BMI (OR 1.02 per kg/m², 95% CI 0.90-1.16) showed meaningful associations (both $P>0.5$).

Discussion

The main goals of this study were to examine the association between echocardiographic parameters of RV systolic and diastolic function in patients with non-

obstructive CAD. Our results indicate that the RV E/e' ratio was significantly elevated in the mAlb (+) group compared to the mAlb (-) group. Also, our analysis demonstrates that microalbuminuria independently predicts elevated RV filling pressure (adjusted OR 2.88, 95% CI 1.22-6.84), even after adjustment for age, sex, and BMI. The RV E/e' ratio is a critical echocardiographic measure for evaluating RV diastolic function, calculated from the early diastolic velocity of the tricuspid inflow (E wave) and the early diastolic velocity of the RV tissue (e' wave). E Wave represents the early filling of the ventricle during diastole, reflecting left atrial pressure and e' Wave reflects the velocity of the myocardial tissue during early diastole, providing insight into the compliance of the ventricle. A higher RV E/e' ratio indicates impaired diastolic function and can suggest elevated right atrial pressure. This may serve as a marker for adverse outcomes in conditions such as heart failure, pulmonary hypertension, and other cardiac diseases, particularly in the assessment of HF with preserved ejection fraction (HFpEF) patients (22). Our results suggest a potential link between renal function and RV diastolic impairment in this population. Interestingly, we did not observe a significant correlation between microalbuminuria and other parameters of RV systolic function, indicating that while diastolic function is affected by microalbuminuria, systolic function remains

relatively preserved in individuals with non-obstructive CAD (23).

Insights from Existing Literature and Clinical Implications of RV E/e' Ratio

The E wave reflects the velocity of the RV sidewall myocardial tissue during the initial phase of diastole (24). We evaluated RV filling during early diastole, calculating the ratio of the peak velocity of early diastolic flow across the tricuspid valve (E) to the peak velocity of early diastolic motion of the tricuspid annulus (e'). The RV E/e' ratio - derived from dividing E-wave velocity by tissue Doppler-measured lateral tricuspid annular e' velocity - serves as a validated non-invasive measure of RV filling pressures, with elevated values (>6) indicating diastolic dysfunction (20). When RV compliance, relaxation, and filling pressures are normal, typical myocardial function leads to a standard lateral e' velocity, resulting in a low E/e' ratio. Conversely, impaired RV diastolic function and elevated filling pressures lead to reduced e' velocities, which, combined with increased right atrial pressure (RAP), elevate the trans-tricuspid E velocity and subsequently the E/e' ratio. Despite being recommended in various ASE guidelines for estimating RAP, the RV E/e' ratio is not widely utilized, despite its simplicity in acquisition and calculation (19, 25). Furthermore, it has been included in the 2020 right heart assessment guidelines by the British Society of Echocardiography as a measure for evaluating RV diastolic function (26).

Elevated urine albumin levels are among the earliest indicators of chronic kidney disease (CKD) and renal microvascular damage and glomerular dysfunction (27). Early screening for high urine albumin, coupled with proactive patient management, can significantly reduce the risk of progression to end-stage renal disease (ESRD) and mitigate associated cardiovascular morbidity, including ischemic events, arrhythmias, and particularly HF (28). This clinical approach has gained particular importance with the advent of renoprotective therapies that concurrently reduce albuminuria while offering dual cardiorenal protection.

Previous research has primarily focused on the relationship between albuminuria and LV function, with fewer studies examining RV function specifically. For example, Katz et al. (2014) explored both right and LV function in patients with HFpEF and identified significant correlations between RVFAC and RV wall thickness (RVWT) with albuminuria (29). Their study found that the UACR was higher in patients exhibiting abnormal RVFAC or RVWT, although no association was noted between albuminuria and TAPSE. In our study, while we observed similar results regarding TAPSE, we did not find a relationship between RVFAC and albuminuria. This discrepancy may stem from variations in study populations or the specific characteristics of our cohort, which mainly included non-obstructive CAD patients.

In a broader context, it is plausible that RV diastolic dysfunction may occur earlier with microalbuminuria, while RV systolic dysfunction might emerge later as macroalbuminuria develops. This aligns with findings

from Jørgensen et al. (2018), which indicated a correlation between microalbuminuria and diastolic dysfunction, enhancing our understanding of the interplay between renal and cardiac functions in CAD patients (30). Although Katz et al. (2014) reported disturbances in RV systolic parameters among HFpEF patients with microalbuminuria (29), our study did not replicate these correlations, suggesting that the underlying pathophysiological mechanisms may differ significantly across populations and warrant further exploration.

Analysis of NHANES data (n=1,214 adults with HF) revealed a 22.1% prevalence of microalbuminuria. After multivariable adjustment, HF patients demonstrated 1.89-fold higher odds of albuminuria compared to non-HF controls, suggesting significant cardiorenal interplay (31). Similarly, elevated normal UACR levels (<30 mg/g) were associated with an increased risk of HF in 10,975 participants from the ARIC (Atherosclerosis Risk in Communities) study (32). Analysis revealed a dose-dependent relationship between albuminuria and HF risk. Compared to the reference group (UACR <5 mg/g), adjusted hazard ratios increased progressively across subthreshold albuminuria categories (5–9 mg/g: HR 1.54; 10–29 mg/g: HR 1.91). Clinically significant albuminuria demonstrated even stronger associations, with microalbuminuria (HR 2.49) and macroalbuminuria (HR 3.47) remaining independent of both CAD and estimated GFR in multivariable models. In patients with HFpEF, elevated UACR was associated with impaired systolic function and greater right and left ventricular remodeling (29). Diabetic patients with persistent microalbuminuria demonstrated concurrent evidence of diffuse cardiac impairment, including diastolic dysfunction (30, 33). Even subclinical albuminuria (<30 mg/g) correlated with left ventricular hypertrophy and diastolic dysfunction in hypertensive individuals, with a more pronounced association in patients aged <70 years. (34). Albuminuria has significant prognostic implications for individuals with HF. One study found that higher admission UACR levels were significantly associated with a greater likelihood of HF readmission (35). A meta-analysis of eleven studies involving HF patients demonstrated an increase in all-cause mortality associated with both micro- and macroalbuminuria (36).

The relationship between microalbuminuria and ventricular function is complex. Microalbuminuria can arise from ventricular dysfunction, and albuminuria has been linked to ventricular dysfunction even before the onset of HF (30, 32). This suggests that factors such as endothelial dysfunction and systemic inflammation may mediate the connection between albuminuria and cardiac dysfunction. Additionally, severe RV dysfunction can lead to increased pressure in the venous system, resulting in renal congestion. This congestion can affect kidney function and contribute to albuminuria (37-39).

The high incidence of microalbuminuria in our patients may be attributed to various population characteristics, including predisposing conditions such as HTN, DM, and CKD. These comorbidities are often intertwined, creating a complex clinical picture where each condition exacerbates the others.

Mechanistic Links & Clinical Implications

Our findings demonstrate microalbuminuria as an independent predictor of elevated RV filling pressure (adjusted OR 2.88, 95% CI 1.22-6.84), unaffected by traditional risk factors (sex, age, BMI), suggesting unique pathophysiological pathways linking renal and cardiac dysfunction. This association likely involves either venous congestion-mediated renal injury from retrograde pressure transmission or shared neurohormonal activation through RAAS/sympathetic pathways, supporting the clinical utility of albuminuria screening (with effect size comparable to echocardiographic parameters) for early detection of right heart dysfunction in at-risk populations. The clinical implications of these findings are significant. Identifying microalbuminuria in non-obstructive CAD patients may indicate the need for closer monitoring and more aggressive management of cardiovascular risk factors. Since microalbuminuria often precedes overt renal impairment and cardiovascular events, it could serve as a valuable screening tool in clinical practice. Early detection and intervention may help mitigate the progression of both renal and cardiovascular diseases, ultimately improving patient outcomes.

Limitations of the Study

Being observational, the study does not establish a causal relationship between albuminuria and echocardiographic findings of right-sided HF. Additionally, using a single urine sample to measure UACR may reduce the reliability of the results (40). The lack of longitudinal data on albuminuria, creatinine, or blood pressure restricts our ability to comprehend how variations in these parameters may affect the relationship over time. Longitudinal studies are warranted to further elucidate this relationship and assess whether interventions targeting microalbuminuria can improve cardiac outcomes. This study did not assess lipid profiles (e.g., cholesterol, triglycerides) or hyperlipidemia status, which may be relevant to certain clinical outcomes. Moreover, our assessment of RV hemodynamics was limited to filling pressure estimation via the E/e' ratio rather than comprehensive diastolic assessment. Cardiac MRI or speckle-tracking echocardiography could provide more detailed insights into myocardial mechanics and improve our comprehension of how microalbuminuria affects RV performance.

Conclusion

Our analysis demonstrates that microalbuminuria serves as an independent predictor of elevated RV filling pressure in non-obstructive CAD patients, suggesting its potential role as an early marker of subclinical RV dysfunction. These findings highlight the value of routine albuminuria screening in cardiac risk assessment. Further research should investigate the underlying mechanisms and potential benefits of early intervention in microalbuminuric patients.

Authors' Contributions

Study conception and design: EE, MR
Data acquisition: EE

Data analysis and interpretation: EE, MR, AA
Manuscript drafting: AA, KR, ShA
Critical revision for intellectual content: MR, AA
Final approval of manuscript: All authors
Each author has reviewed the manuscript and agrees to be accountable for all aspects of the work.

Ethical Considerations

The study received approval from the Ethics Committee of Qazvin University of Medical Sciences (IR.QUMS.REC.1399.208), and written informed consent was obtained from all participants.

Acknowledgment

We thank all nurses of BouAli Hospital of Qazvin University of Medical Sciences for their kind cooperation.

Conflict of Interests

The authors declare that they have no competing interests.

References

1. Klausen K, Scharling H, Jensen J. Very low level of microalbuminuria is associated with increased risk of death in subjects with cardiovascular or cerebrovascular diseases. *J Intern Med.* 2006;260(3):231-7.
2. Gross JL, De Azevedo MJ, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic nephropathy: diagnosis, prevention, and treatment. *Diabetes Care.* 2005;28(1):164-76.
3. Valmadrid CT, Klein R, Moss SE, Klein BE. The risk of cardiovascular disease mortality associated with microalbuminuria and gross proteinuria in persons with older-onset diabetes mellitus. *Arch Intern Med.* 2000;160(8):1093-100.
4. Matsushita K, Coresh J, Sang Y, Chalmers J, Fox C, Guallar E, et al. Estimated glomerular filtration rate and albuminuria for prediction of cardiovascular outcomes: a collaborative meta-analysis of individual participant data. *Lancet Diabetes Endocrinol.* 2015;3(7):514-25.
5. Scirica BM, Mosenzon O, Bhatt DL, Jacob AU, Steg PG, McGuire DK, et al. Cardiovascular outcomes according to urinary albumin and kidney disease in patients with type 2 diabetes at high cardiovascular risk: observations from the SAVOR-TIMI 53 trial. *JAMA Cardiol.* 2018;3(2):155-63.
6. Holtkamp FA, De Zeeuw D, De Graeff PA, Laverman GD, Berl T, Remuzzi G, et al. Albuminuria and blood pressure, independent targets for cardioprotective therapy in patients with diabetes and nephropathy: a post hoc analysis of the combined RENAAL and IDNT trials. *Eur Heart J.* 2011;32(12):1493-9.
7. Zandbergen AA, Vogt L, Dick de Zeeuw M, Lamberts SW, Ouwendijk RJ, Baggen MG, et al. Change in albuminuria is predictive of cardiovascular outcome in normotensive patients with type 2 diabetes mellitus and microalbuminuria. *Diabetes Care.* 2007;28(5):1157-63.
8. Toyama T, Furuichi K, Ninomiya T, Shimizu M, Hara A, Iwata Y, et al. The impacts of albuminuria and low eGFR on the risk of cardiovascular death, all-cause mortality, and renal events in diabetic patients: meta-analysis. *PLoS One.* 2013;8(8):e71810.
9. Jackson CE, MacDonald MR, Petrie MC, Solomon SD, Pitt B, Latini R, et al. Associations of albuminuria in patients with chronic heart failure: findings in the ALiSkiren Observation of heart Failure Treatment study. *Eur J Heart Fail.* 2011;13(7):746-54.
10. de Jong PE, Gansevoort RT, Bakker SJ. Macroalbuminuria and microalbuminuria: do both predict renal and cardiovascular events with similar strength? *J Nephrol.* 2007;20(4):375.
11. Yurtdas M, Ozdemir M, Aladag N, Yaylali YT. Association of heart rate recovery with microalbuminuria in non-obstructive coronary artery disease. *Cardiol Res.* 2017;8(5):206.
12. Homayounfar S, Khansari N, Fariba F. Echocardiographic Evaluation of Indices of Right Ventricle Dysfunction in Pulmonary Hypertension. *Avicenna J Clin Med.* 2017;23(4):281-7.
13. Konstam MA, Kiernan MS, Bernstein D, Bozkurt B, Jacob M, Kapur NK, et al. Evaluation and management of right-sided heart fail-

ure: a scientific statement from the American Heart Association. *Circulation*. 2018;137(20):e578-e622.

14. Djoussé L, Kochar J, Hunt SC, North KE, Gu CC, Tang W, et al. Relation of albuminuria to left ventricular mass (from the HyperGEN Study). *Am J Cardiol*. 2008;101(2):212-6.

15. Targher G, Mantovani A, Wang X-B, Yan H-D, Sun Q-F, Pan K-H, et al. Patients with diabetes are at higher risk for severe illness from COVID-19. *Diabetes Metab*. 2020;46(4):335.

16. Flack JM, Adekola B. Blood pressure and the new ACC/AHA hypertension guidelines. *Trends Cardiovasc Med*. 2020;30(3):160-4.

17. Fiseha T, Mengesha T, Girma R, Kebede E, Gebreweld A. Estimation of renal function in adult outpatients with normal serum creatinine. *BMC Res Notes*. 2019;12(1):462.

18. Douglas PS, Garcia MJ, Haines DE, Lai WW, Manning WJ, Patel AR, et al. ACCF/ ASE/AHA/ ASNC/ HFSA/HRS/ SCAI/SCCM/ SCCT/ SCMR 2011 appropriate use criteria for echocardiography. *J Am Coll Cardiol*. 2011;57(9):1126-66.

19. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography: endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr*. 2010;23(7):685-713.

20. Caballero L, Kou S, Dulgheru R, Gonjilashvili N, Athanassopoulos GD, Barone D, et al. Echocardiographic reference ranges for normal cardiac Doppler data: results from the NORRE Study. *Eur Heart J Cardiovasc Imaging*. 2015;16(9):1031-41.

21. Willis J, Augustine D, Shah R, Stevens C, Easaw J. Right ventricular normal measurements: time to index? *J Am Soc Echocardiogr*. 2012;25(12):1259-67.

22. Yogeswaran A, Rako ZA, Yildiz S, Ghofrani HA, Seeger W, da Rocha BB, et al. Echocardiographic evaluation of right ventricular diastolic function in pulmonary hypertension. *ERJ Open Res*. 2023;9(5):00226-2023.

23. Jung Y-H, Ren X, Suffredini G, Dodd-o JM, Gao WD. Right ventricular diastolic dysfunction and failure: a review. *Heart Fail Rev*. 2022;27(4):1077-90.

24. Maragiannis D, Nagueh SF. Evaluation of right ventricular diastolic function. *Diastology E-Book: Clinical Approach to Heart Failure with Preserved Ejection Fraction*. 2020:180.

25. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging*. 2015;16(3):233-71.

26. Zaidi A, Knight DS, Augustine DX, Harkness A, Oxborough D, Pearce K, et al. Echocardiographic assessment of the right heart in adults: a practical guideline from the British Society of Echocardiography. *Echo Res Pract*. 2020;7(1):G19-G41.

27. Zhang J, Deng Y, Wan Y, He S, Cai W, Xu J. Association between serum albumin level and microvascular complications of type 2 diabetes mellitus. *Diabetes Metab Syndr Obes*. 2022;2173-82.

28. Rossing P, Caramori ML, Chan JC, Heerspink HJ, Hurst C, Khunti K, et al. KDIGO 2022 clinical practice guideline for diabetes management in chronic kidney disease. *Kidney Int*. 2022;102(5):S1-S127.

29. Katz DH, Burns JA, Aguilar FG, Beussink L, Shah SJ. Albuminuria is independently associated with cardiac remodeling, abnormal right and left ventricular function, and worse outcomes in heart failure with preserved ejection fraction. *JACC Heart Fail*. 2014;2(6):586-96.

30. Jørgensen PG, Biering-Sørensen T, Mogelvang R, Fritz-Hansen T, Vilsbøll T, Rossing P, et al. Presence of micro- and macroalbuminuria and the association with cardiac mechanics in patients with type 2 diabetes. *Eur Heart J Cardiovasc Imaging*. 2018;19(9):1034-41.

31. Odutayo A, Hsiao AJ, Emdin CA. Prevalence of albuminuria in a general population cohort of patients with established chronic heart failure. *J Card Fail*. 2016;22(1):33-7.

32. Blecker S, Matsushita K, Köttgen A, Loehr LR, Bertoni AG, Boulware LE, et al. High-normal albuminuria and risk of heart failure in the community. *Am J Kidney Dis*. 2011;58(1):47-55.

33. Swoboda PP, McDiarmid AK, Erhayem B, Ripley DP, Dobson LE, Garg P, et al. Diabetes mellitus, microalbuminuria, and subclinical cardiac disease: identification and monitoring of individuals at risk of heart failure. *J Am Heart Assoc*. 2017;6(7):e005539.

34. Wang T, Zhong H, Lian G, Cai X, Gong J, Ye C, et al. Low-grade albuminuria is associated with left ventricular hypertrophy and diastolic dysfunction in patients with hypertension. *Kidney Blood Press Res*. 2019;44(4):590-603.

35. Matsumoto Y, Orihara Y, Asakura M, Min KD, Okuhara Y, Azuma K, et al. Urine albumin-to-creatinine ratio on admission predicts early rehospitalization in patients with acute decompensated heart failure. *Heart Vessels*. 2022:1-11.

36. Mehta R, Ning H, Bansal N, Cohen J, Srivastava A, Dobre M, et al. Ten-year risk-prediction equations for incident heart failure hospitalizations in chronic kidney disease: findings from the Chronic Renal Insufficiency Cohort Study and the Multi-Ethnic Study of Atherosclerosis. *J Card Fail*. 2022;28(4):540-50.

37. Ataga KI, Derebail VK, Caughey M, Elsherif L, Shen JH, Jones SK, et al. Albuminuria is associated with endothelial dysfunction and elevated plasma endothelin-1 in sickle cell anemia. *PLoS One*. 2018;11(9):e0162652.

38. Martens RJ, Houben AJ, Kooman JP, Berendschot TT, Dagnelie PC, van der Kallen CJ, et al. Microvascular endothelial dysfunction is associated with albuminuria: the Maastricht Study. *J Hypertens*. 2018;36(5):1178-87.

39. Zuchi C, Tritto I, Carluccio E, Mattei C, Cattadori G, Ambrosio G. Role of endothelial dysfunction in heart failure. *Heart Fail Rev*. 2020;25(1):21-30.

40. Levey AS, Eckardt K-U, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int*. 2005;67(6):2089-100.