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ORIGINAL ARTICLE
Vascular and cardiac imaging

Prevalence of albuminuria and its association with left atrial remodelling in patients with atrial fibrillation

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Aims

Although recent epidemiological studies identified albuminuria as an independent risk for atrial fibrillation (AF), even in individuals with a preserved or mildly reduced estimated glomerular filtration rate (eGFR), the prevalence of albuminuria and its association with left atrial (LA) remodelling in patients with AF remains unknown. This study aimed to investigate the association of albuminuria with LA structure and mechanics before and after catheter ablation (CA) in AF patients.

Methods and results

We examined 133 AF patients with an eGFR ≥60 mL/min/1.73 m^2 who underwent first CA. Conventional and speckle-tracking echocardiography was performed before and 6 months after CA to assess the LA volume index, LA reservoir strain, and LA stiffness. The median eGFR was 70 mL/min/1.73m^2, and 21 (15.8%) patients had albuminuria. The difference between the eGFR values of patients with and without albuminuria was not significant ($P = 0.709$). Patients with albuminuria had a larger LA volume index, reduced LA reservoir strain and increased LA stiffness compared with patients without albuminuria (all $P < 0.001$). The presence of albuminuria was associated with reduced LA reservoir strain and increased LA stiffness, independent of age, AF type, and AF risk factors. After CA, there was significant improvement in LA size and function in both groups, while albuminuria group still had a larger LA volume index and increased LA stiffness (both $P < 0.05$).

Conclusion

Approximately 16% of AF patients with preserved or mildly reduced eGFR had albuminuria. The presence of albuminuria was related to unfavourable LA remodelling and its persistence even after restoration of sinus rhythm.

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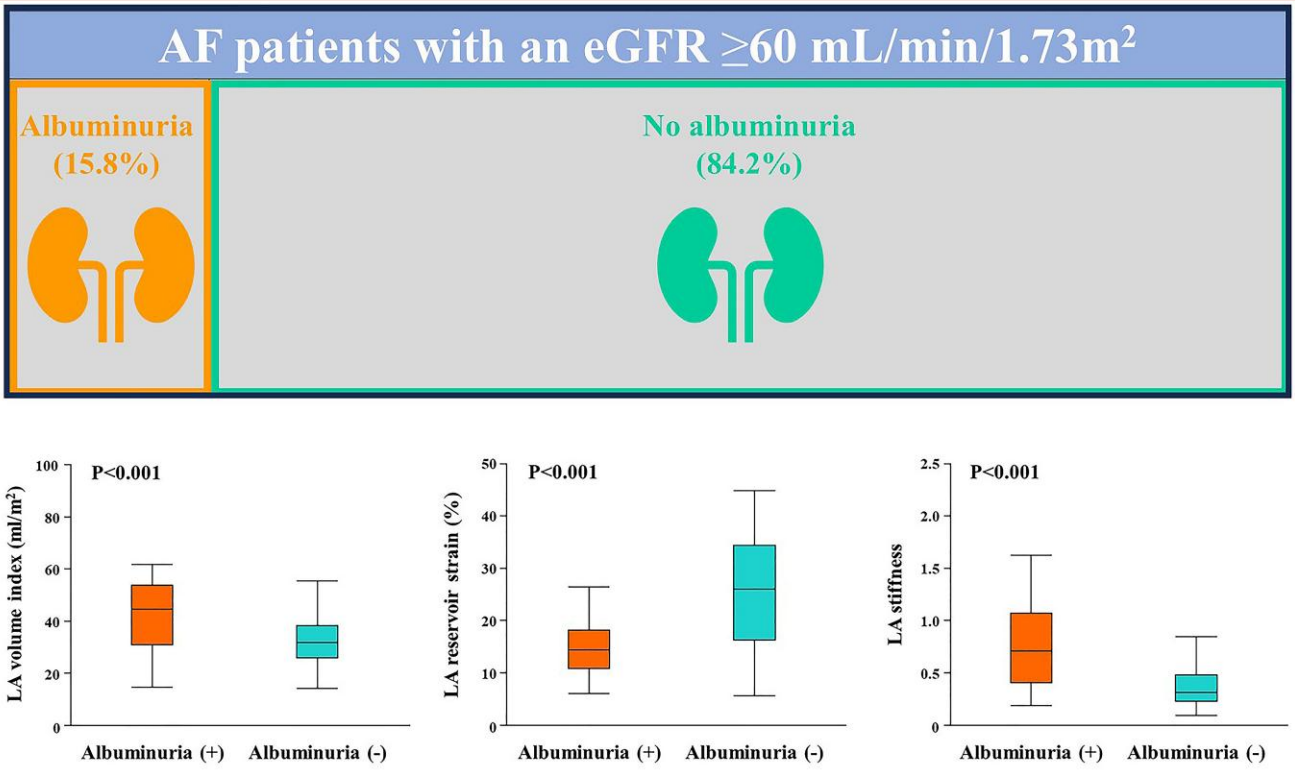
Graphical abstract



Association of albuminuria with LA morphology and function

	LA volume index		LA reservoir strain		LA stiffness	
	Sβ (95% CI)	p value	Sβ (95% CI)	p value	Sβ (95% CI)	p value
Model 1	0.29 (2.03 to 7.65)	<0.001	-0.31 (-6.79 to -2.03)	<0.001	0.40 (0.11 to 0.35)	<0.001
Model 2	0.14 (-0.05 to 5.16)	0.055	-0.16 (-4.15 to -0.21)	0.030	0.28 (0.06 to 0.19)	<0.001
Model 3	0.15 (-0.02 to 5.21)	0.052	-0.17 (-4.29 to -0.36)	0.021	0.28 (0.06 to 0.19)	<0.001
Model 4	0.13 (-0.61 to 4.84)	0.127	-0.08 (-3.09 to 0.77)	0.237	0.22 (0.04 to 0.16)	0.003
Model 5	-	-	-0.03 (-2.38 to 1.23)	0.529	0.19 (0.02 to 0.15)	0.008

Model 1: age and sex adjusted.

Model 2: adjusted for age, sex, AF type, BMI, hypertension, diabetes mellitus, dyslipidemia and current smoking.

Model 3: adjusted for variables as in Model 2, eGFR and CRP levels.

Model 4: adjusted for variables as in Model 3, LV mass index, LV ejection fraction and e' velocity.

Model 5: adjusted for variables as in Model 4 and LA volume index.

Keywords albuminuria • Atrial fibrillation • Left atrial remodelling

Introduction

Atrial fibrillation (AF) is the most common and progressive rhythm disorder encountered in daily practice, and its prevalence is increasing with the aging population. Chronic kidney disease, often defined by an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 in routine clinical practice, carries a significant and independent risk for AF occurrence;[1,2] although more than 50% of patients with AF have a normal or mildly reduced eGFR (≥60 mL/min/1.73 m^2).[3,4] Recent epidemiological studies have shown that albuminuria is associated with the development of AF in the general population independent of eGFR values.[1,5,6] In addition, albuminuria is also related to subsequent ischaemic stroke and heart failure;[7,8] however, the underlying pathophysiological mechanisms are unknown.

Left atrial (LA) structural and functional changes play a pivotal role in the development and progression of AF.[9,10] The novel imaging modality, speckle-tracking echocardiography (STE), enables objective and quantitative assessment of LA function.[11–13] Impairment of LA reservoir strain on STE precedes LA enlargement and is an accurate predictor for AF, as well as stroke and heart failure.[14–17] More recently, echocardiography-derived LA stiffness was introduced and exhibited a good correlation with invasively obtained LA stiffness and AF risk score.[18,19] However, the exact prevalence of albuminuria and its association with LA morphology and function in patients with AF is unknown. We hypothesized that AF patients with albuminuria had more advanced LA remodelling even with normal or mildly reduced eGFR. Accordingly, the aim of this study was to investigate the prevalence of albuminuria and its relationship with LA size and function before and after catheter ablation (CA) in AF patients with eGFR $\geq$ 60 mL/min/1.73 m^2.

Methods

Study population

This study included 133 consecutive AF patients with an eGFR $\geq$ 60 mL/min/1.73 m^2 who underwent urinalysis for the evaluation of albuminuria and first CA between May 2019 and March 2022 at the University of Tokyo Hospital. The exclusion criteria were as follows: (i) congenital heart disease, (ii) moderate or severe valvular disease, (iii) dilated or hypertrophic cardiomyopathy, (iv) history of cardiothoracic surgery within 3 months, and (v) history of pacemaker implantation. AF was defined as 'paroxysmal' when the arrhythmia self-terminated within 7 days, and 'persistent' when the AF episode persisted for 7 days or pharmacological or electrical cardioversion was required to terminate the arrhythmia.[20] All study participants provided written informed consent. The investigation conformed to the principles outlined in the Declaration of Helsinki, and the study was approved by the institutional ethics committee of the University of Tokyo (2018120NI).

Risk factors and laboratory examination

Hypertension was defined as systolic blood pressure $\geq$ 140 mm Hg, or diastolic blood pressure $\geq$ 90 mm Hg, or the use of antihypertensive drugs. Diabetes mellitus was defined by a fasting blood glucose level of $\geq$ 126 mg/dL or current use of insulin or hypoglycaemic agents. Dyslipidemia was defined as total serum cholesterol > 240 mg/dL or the use of lipid lowering medications. Body mass index (BMI) was calculated as body weight (kg) divided by height-squared (m^2). All blood samples were collected with patients in the sitting position, and measurements included fasting glucose, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, C-reactive protein, and B-type natriuretic peptide (BNP). The eGFR was calculated by the abbreviated Modification of Diet in Renal Disease formula: eGFR (mL/min/1.73 m^2) = $194 \times (\text{serum creatinine})^{-1.094} \times (\text{age})^{-0.287} \times (0.739$ if woman). The urine albumin-to-creatinine ratio (UACR) was calculated as follows: UACR (mg/gCr) = urinary albumin (mg/dL)/urinary creatinine (mg/dL) $\times$ 1000. We used the following reagents: urinary creatinine was measured using an enzyme assay (L-type Wako CRE • M; FUJIFILM Wako Pure Chemical, Osaka, Japan), and microalbumin was measured using a turbidimetric immunoassay (Auto Wako microalbumin; FUJIFILM Wako). According to the UACR values, patients were classified into the following groups: normal-range albuminuria (< 30 mg/gCr), microalbuminuria (30–300 mg/gCr), and macroalbuminuria (> 300 mg/gCr). Albuminuria was diagnosed when either micro- or macroalbuminuria was present.

Conventional echocardiography

Transthoracic echocardiography was performed by a commercially available system, Vivid E95 (GE Vingmed Ultrasound, Horten, Norway) or EPIQ 7 (Koninklijke Philips N.V., Netherlands), 1–4 days before and 6 months after CA. All images were acquired according to a standardized protocol by experienced and registered cardiologists. The dimensions of the cardiac chambers were measured in the standard manner.[21] Left ventricular (LV) mass was calculated by a validated Devereux's formula, as follows:[21] LV mass = $0.8\ \{1.04[(\text{SWT} + \text{LVEDD} + \text{PWT})^3 - \text{LVEDD}^3]\} + 0.6$, where SWT = LV end-diastolic septal wall thickness, LVEDD = LV end-diastolic diameter, and PWT = LV end-diastolic posterior wall thickness. Left atrial (LA) volume was measured from the apical 2- and 4-chamber views, using the biplane Simpson's rule.[21] LV mass and LA volume were indexed for body surface area. Pulsed-wave Doppler examination of mitral inflow was performed to measure early peak velocity (E). Peak early diastolic mitral annular velocity (e′) was also measured from tissue Doppler imaging in the septal and lateral mitral annulus. The ratio of E to mean e′ was then calculated (E/e′). The maximum and minimum inferior vena cava (IVC) diameters were measured at 1.0 to 2.0 cm from the junction with the right atrium.[21] IVC collapsibility index was calculated as follows: (maximum IVC − minimum IVC)/maximum IVC $\times$ 100.

Assessment of LA function and stiffness

Speckle-tracking analysis was performed off-line with the use of vendor-independent and commercially available software (2D Cardiac Performance Analysis; Tomtec Imaging System, Germany). Semi-automated border detection was performed, and the LA border was tracked throughout the cardiac cycle. Manual correction was performed in cases of inadequate endocardial detection. LA reservoir strain was obtained by averaging peak values of 6 LA segmental strains from apical 2– and 4– chamber views, with the onset of the QRS complex used as the zero-reference point (R-R gating), according to guideline recommendations.[11,12] Excellent inter-observer variability for LA strain measurement was found in 15 randomly selected patients (intraclass correlation coefficient = 0.93) by two independent and blinded observers. LA stiffness was also estimated from the ratio of E/e′ to LA reservoir strain.[19,22]

CA procedures and follow-up

CA was performed with the patient under sedation. All patients underwent pulmonary vein isolation (PVI) by point-by-point radiofrequency energy or the balloon technique to restore sinus rhythm, with an endpoint of bidirectional block between the LA and the inside of the circumferential PVI area. Additional procedures, including cavotricuspid isthmus ablation, superior vena cava isolation, roof line and mitral isthmus line ablation, were performed at the physician's discretion. After the CA procedure, patients were evaluated every 1 to 2 months at the outpatient clinic. A 12-lead electrocardiogram was carried out at each follow-up visit, and 24-h Holter monitoring was performed 3 to 6 months after the procedure. Recurrence of arrhythmia was defined as any episode of atrial arrhythmia that lasted longer than 30 s on a 12-lead electrocardiogram or Holter monitoring after a 2-month blanking period from the date of CA.

Statistical analysis

Continuous variables are expressed as means ± standard deviation or medians with interquartile range and were compared by an unpaired Student's *t*-test or Wilcoxon rank sum test, as appropriate. Categorical variables are presented as numbers and proportions and were compared by the chi-squared or Fisher exact tests. Baseline characteristics, including laboratory parameters and echocardiographic findings, were compared between patients with and without albuminuria. Univariable and multivariable linear regression analyses were carried out to identify an independent association of abnormal UACR with LA morphology and function, with adjustments for potential covariates in sequential fashion in 5 models. The corresponding odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Model 1: adjustment for age and sex; Model 2: adjustment for age, sex, AF type, BMI, hypertension, diabetes mellitus, dyslipidemia, and current smoking; Model 3: adjustment as in model 2 plus eGFR and CRP levels; Model 4: adjustment as in model 3 plus pertinent echocardiographic parameters, including LV mass index, LV ejection fraction and e′ velocity; Model 5: adjustment as in model 4 plus LA volume index (only for LA reservoir strain and LA stiffness). LA volume index was put in the model 5 because LA size was also set as one of the dependent variables in the multivariable analyses to elucidate the association between UACR and LA structural change. A value of $P < 0.05$ was considered significant. Statistical analyses were performed using JMP 14 software (SAS Institute, Cary, NC, USA).

Results

Patient characteristics and prevalence of albuminuria

The median age was 64 (25th–75th percentile, 54–71) years, and 101 (75.9%) of the patients were men. AF was paroxysmal in 78 patients (58.6%) and persistent in 55 patients (41.4%). The median eGFR was 70 (25th–75th percentile, 64–79) mL/min/1.73 m^2, and all study participants had an eGFR ≥ 60 mL/min/1.73 m^2 by virtue of the study design. Among the study participants, 21 (15.8%) patients had albuminuria (20 with microalbuminuria and 1 with macroalbuminuria; *Figure 1A*). The clinical characteristics of the study population stratified by the presence or absence of albuminuria are summarized in *Table 1*. Patients with albuminuria were older, with a higher prevalence of persistent AF and diabetes mellitus (all $P < 0.05$), compared with patients without albuminuria, while other AF risk factors were not. As for the laboratory parameters, circulating BNP levels were higher in albuminuria group ($P < 0.05$). There was no significant difference in eGFR values between patients with and without albuminuria [69 (64–76) vs. 71 (64–80) mL/min/1.73 m^2, $P = 0.709$].

Albuminuria and LA remodelling

Table 2 shows the echocardiographic parameters. There were no significant differences in LV size and LV mass index between patients with and without albuminuria, whereas lower LV ejection fraction and higher E/e′ ratio were observed in albuminuria group (both $P < 0.05$). In terms of LA parameters, patients with albuminuria had the larger LA volume index [44.5 (31.0–53.7) vs. 31.7 (25.8–38.5) mL/m^2, $P < 0.001$] and reduced LA reservoir strain [14.4 (10.7–18.1) vs. 26.1 (16.3–34.3) %, $P < 0.001$] and increased LA stiffness [0.71 (0.40–1.07) vs. 0.31 (0.23–0.48), $P < 0.001$; *Figure 2*].

Results of multivariable linear regression analyses to investigate the association of albuminuria with LA morphology and function are shown in *Table 3*. Albuminuria was significantly associated with LA volume index, LA reservoir strain, and LA stiffness in the age- and sex-adjusted model (all $P < 0.001$, Model 1). The multivariable model adjusted for age, sex, AF type, BMI, hypertension, diabetes mellitus, dyslipidemia and current smoking attenuated the association between albuminuria and LA size (standardized β 0.14, $P = 0.055$); whereas the presence of albuminuria was related to reduced LA reservoir strain and increased LA stiffness (*Table 3*, Model 2). This relationship persisted after additional adjustments for laboratory measures (i.e. eGFR and CRP levels; *Table 3*, Model 3). With further adjustments for echocardiographic parameters, including LV mass index, LV ejection fraction, e′ velocity and LA volume index, the association between albuminuria and LA stiffness remained significant (*Table 3*, Models 4 and 5); while the association between albuminuria and LA reservoir strain was diminished. Representative cases are shown in *Figure 1B*. The upper case with albuminuria (UACR 100.0 mg/gCr) had reduced LA reservoir strain compared with the lower case without albuminuria (UACR 3.7 mg/gCr).

Albuminuria and LA remodelling after CA

Among the 133 patients included in the study, 121 underwent follow-up echocardiography at 6 months after CA. Seventeen patients developed recurrent AF within 6 months; the difference between rates of recurrence in the patients with and without albuminuria was not significant (15.0% vs. 13.9%, respectively, $P = 0.894$). There was significant improvement in LA size and function in both patient groups (all $P < 0.01$), while patients with albuminuria still had a significantly larger LA volume index [35.1 (27.8–40.3) vs. 28.7 (22.7–35.9) mL/m^2, $P = 0.034$] and higher LA stiffness [0.31 (0.23–0.42) vs. 0.23 (0.19–0.30), $P = 0.011$] compared with those without albuminuria (*Figure 3*).

A sensitivity analysis of the patients without recurrent AF ($n = 104$) showed results similar to the entire population in which albuminuria group exhibited larger LA size [33.5 (27.9–40.2) vs. 28.4 (22.4–35.5) mL/m^2, $P = 0.036$] and increased LA stiffness [0.28 (0.22–0.39) vs. 0.23 (0.18–0.28), $P = 0.018$] than no-albuminuria group. The data of UACR at 6 months after CA was available in 116 patients, and there was a significant improvement of UACR after CA [10.4 (5.2 to 22.2) mg/gCr to 7.4 (4.1 to 16.4) mg/gCr, $P = 0.022$].

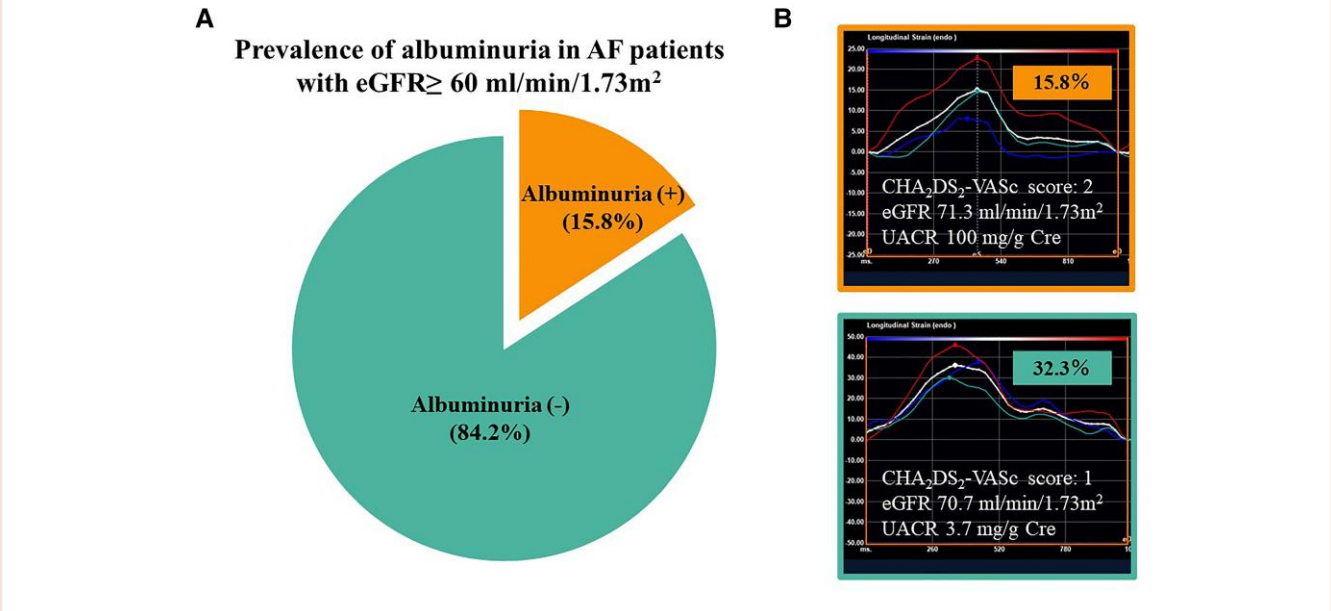


Figure 1 Prevalence of albuminuria (*A*) and representative images of LA reservoir strain in patients with and without albuminuria (*B*). AF, atrial fibrillation; eGFR, estimated glomerular filtration rate; LA, left atrium.

Table 1 Baseline characteristics of the study population

	Albuminuria (+) ($n = 21$)	Albuminuria (−) ($n = 112$)	*P* value
Age, years	71 (61–74)	64 (54–69)	0.019
Men, *n* (%)	18 (85.7)	83 (74.1)	0.404
Persistent AF, *n* (%)	14 (66.7)	41 (36.6)	0.015
Body mass index, kg/m^2	24.0 (22.4–26.0)	24.2 (21.7–27.0)	0.904
Hypertension, *n* (%)	13 (61.9)	50 (44.6)	0.161
Diabetes mellitus, *n* (%)	9 (42.9)	18 (16.1)	0.014
Dyslipidemia, *n* (%)	11 (52.4)	41 (36.6)	0.224
Current smoking, *n* (%)	3 (14.3)	12 (10.7)	0.706
Systolic blood pressure, mmHg	130 (115–140)	120 (108–132)	0.057
Diastolic blood pressure, mmHg	72 (65–80)	66 (60–74)	0.011
Heart rate, beats/min	82 (78–94)	75 (67–83)	0.010
$CHADS_2$ score	1 (1–2)	1 (0–1)	0.004
CHA_2DS_2-VASc score	2 (2–3)	1 (1–2)	0.004
Medications			
β blocker, *n* (%)	10 (47.6)	43 (38.4)	0.472
RAS inhibitor, *n* (%)	8 (38.1)	27 (24.1)	0.188
Calcium channel blocker, *n* (%)	9 (42.9)	37 (33.0)	0.455
Statin, *n* (%)	9 (42.9)	21 (18.8)	0.023
Oral anti-diabetic agents, *n* (%)	8 (38.1)	15 (13.4)	0.011
Insulin, *n* (%)	1 (4.8)	3 (2.7)	0.501
Laboratory data			
Fasting glucose, mg/dL	104 (96–126)	95 (88–102)	<0.001
HbA1c, %	6.1 (5.9–6.7)	5.7 (5.5–6.0)	<0.001
Total cholesterol, mg/dL	181 ± 35	202 ± 38	0.017
LDL cholesterol, mg/dL	107 (82–117)	112 (97–141)	0.126
HDL cholesterol, mg/dL	56 (48–67)	60 (48–76)	0.379
eGFR, mL/min/1.73 m^2	69 (64–76)	71 (64–80)	0.709
B-type natriuretic peptide, pg/mL	152 (63–279)	40 (20–79)	<0.001
C-reactive protein, mg/dL	0.09 (0.05–0.22)	0.06 (0.03–0.10)	0.059
UACR, mg/g Cre	71.9 (43.0–100.0)	7.3 (4.5–13.4)	N/A
Ablation procedure characteristics			
Total procedure time, min	163 (141–230)	165 (145–200)	0.668
PVI, *n* (%)	21 (100.0)	112 (100.0)	N/A
Ablation technique			0.008
Radiofrequency ablation, *n* (%)	17 (81.0)	55 (49.1)	
Cryoballoon ablation, *n* (%)	4 (19.0)	57 (50.9)	
Extensive LA ablation, *n* (%)	3 (14.3)	3 (2.7)	0.050
SVC isolation, *n* (%)	1 (4.8)	2 (1.8)	0.405
Cavotricuspid isthmus, *n* (%)	5 (23.8)	25 (22.3)	0.882

Values are mean ± standard deviation, *n* (percentage), or median (25th–75th percentile).
AF, atrial fibrillation; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LA, left atrium; LDL, low-density lipoprotein; PVI, pulmonary vein isolation; RAS, renin-angiotensin system; SVC, superior vena cava; UACR, urine albumin-to-creatinine ratio.

Discussion

The major findings of this study were as follows: (i) 16% of AF patients with preserved or mildly reduced eGFR had albuminuria, (ii) the presence of albuminuria was significantly associated with LA functional alteration independent of eGFR and AF type, and (iii) CA improved LA structural and functional remodelling, although patients with albuminuria still had larger LA size and increased LA stiffness compared with those without albuminuria.

Recent epidemiological studies clearly demonstrated the association between albuminuria and incident AF, and the relationship was independent of eGFR. Alonso *et al.*[1] found that albuminuria was related to the occurrence of AF during a median follow-up of 10 years in 10 328 individuals from the Atherosclerosis Risk in Communities Study.[1] Marcos *et al.*[5] reported that increased albumin excretion carried an independent risk for the development of AF in 8265 middle-aged subjects.[5] A recent meta-analysis confirmed that the presence of albuminuria was independently associated with increased risk of AF in 28 470 249 participants from 38 studies.[6]

However, the prevalence and clinical significance of the albuminuria in patients with AF remained unclear. We demonstrated for the first time that approximately one-sixth of AF patients with an eGFR ≥

Table 2 Echocardiographic parameters stratified by the presence or absence of albuminuria

	Albuminuria (+) ($n = 21$)	Albuminuria (−) ($n = 112$)	*P* value
LV parameters			
LV end-diastolic diameter, mm	46.2 ± 5.3	46.0 ± 4.6	0.887
LV end-systolic diameter, mm	31.4 (27.4–34.4)	30.0 (26.9–32.8)	0.217
LV ejection fraction, %	57.0 (44.1–66.4)	63.0 (59.0–67.8)	0.008
LV mass index, g/m^2	90.0 ± 18.1	83.8 ± 19.4	0.178
E wave, cm/s	79.7 ± 18.6	70.0 ± 16.7	0.018
e′, cm/s	8.3 (7.5–9.2)	8.7 (7.1–10.7)	0.286
E/e′ ratio	9.8 (7.6–10.9)	7.7 (6.6–9.6)	0.005
LA parameters			
LA volume index, mL/m^2	44.5 (31.0–53.7)	31.7 (25.8–38.5)	<0.001
LA reservoir strain, %	14.4 (10.7–18.1)	26.1 (16.3–34.3)	<0.001
LA stiffness	0.71 (0.40–1.07)	0.31 (0.23–0.48)	<0.001
Maximum IVC diameter, mm	17.6 (12.6–21.7)	12.0 (10.8–15.4)	0.003
Minimum IVC diameter, mm	7.6 (5.1–15.4)	5.6 (4.0–8.3)	0.012
IVC collapsibility index, %	46.1 (30.5–62.7)	53.4 (42.5–63.6)	0.140

Values are mean ± standard deviation or median (25th–75th percentile).
E, early diastolic transmitral flow velocity; e′, early diastolic mitral annular velocity; IVC, inferior vena cava; LA, left atrium; V, left ventricle.

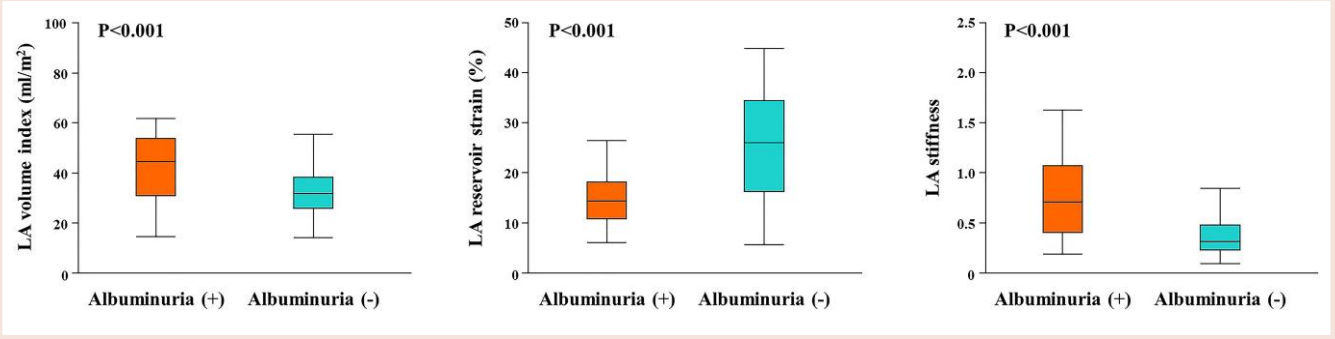


Figure 2 LA volume index, LA reservoir strain, and LA stiffness stratified by the presence or absence of albuminuria before CA. CA, catheter ablation; LA, left atrium.

60 mL/min/1.73 m^2 (usually considered as 'preserved renal function') had albuminuria, and had unfavourable LA structural and functional remodelling. Furthermore, the association between albuminuria and LA functional alteration was independent of age, sex, AF type, and conventional AF risk factors.

Very limited data are available on the association between albuminuria and LA remodelling. Jørgensen *et al.*[23] studied 915 patients with type 2 diabetes and found that those with albuminuria had larger LA size compared with those without albuminuria.[23] Wei *et al.*[24] reported the association between UACR and LA volume index from a post-hoc analysis of the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist Trial.[24] However, to our best knowledge, no study has examined the association between albuminuria and LA remodelling in patients with AF.

The underlying mechanisms by which albuminuria is associated with abnormal LA mechanics in AF patients are not entirely clear; however, there are several plausible explanations. First, enhanced chronic inflammation might be involved in the mechanism linking albuminuria with LA dysfunction.[25,26] Indeed, the serum CRP level in patients with albuminuria tended to be higher than those without albuminuria in the present study. Second, albuminuria is closely related to activation of the renin-angiotensin-aldosterone system, which directly and indirectly leads to LA dysfunction through LV hypertrophy and diastolic dysfunction.[27] Finally, higher UACR values reflect systemic endothelial dysfunction, which has recently been reported to be associated with unfavourable LA remodelling.[28]

Clinical implication

Our observation in the present study may partially explain the increased risk of HF and stroke in AF patients with albuminuria, because LA functional remodelling plays a pivotal role in the pathophysiological mechanisms of heart failure and stroke.[15,17] Patients with albuminuria had larger preprocedural LA size, reduced LA function and increased LA stiffness compared with those without albuminuria. In addition, although improvements in LA size and function were observed in both groups, patients with albuminuria still had a larger LA volume index and greater LA stiffness. These observations suggest that AF patients with albuminuria are more in need of careful follow-up, because persistent LA remodelling is an important risk for AF recurrence and

Table 3 Association of albuminuria with LA morphology and function

	LA volume index		LA reservoir strain		LA stiffness	
	Sβ (95% CI)	*P* value	Sβ (95% CI)	*P* value	Sβ (95% CI)	*P* value
Model 1	0.29 (2.03 to 7.65)	<0.001	−0.31 (−6.79 to −2.03)	<0.001	0.40 (0.11 to 0.35)	<0.001
Model 2	0.14 (−0.05 to 5.16)	0.055	−0.16 (−4.15 to −0.21)	0.030	0.28 (0.06 to 0.19)	<0.001
Model 3	0.15 (−0.02 to 5.21)	0.052	−0.17 (−4.29 to −0.36)	0.021	0.28 (0.06 to 0.19)	<0.001
Model 4	0.13 (−0.61 to 4.84)	0.127	−0.08 (−3.09 to 0.77)	0.237	0.22 (0.04 to 0.16)	0.003
Model 5	—	—	−0.03 (−2.38 to 1.23)	0.529	0.19 (0.02 to 0.15)	0.008

Model 1: age and sex adjusted.
Model 2: adjusted for age, sex, AF type, BMI, hypertension, diabetes mellitus, dyslipidemia and current smoking.
Model 3: adjusted for variables as in Model 2, eGFR and CRP levels.
Model 4: adjusted for variables as in Model 3, LV mass index, LV ejection fraction and e′ velocity.
Model 5: adjusted for variables as in Model 4 and LA volume index.
AF, atrial fibrillation; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; e′, early diastolic mitral annular velocity; eGFR, estimated glomerular filtration rate; LA, left atrium; LV, left ventricle; Sβ, standardized β.

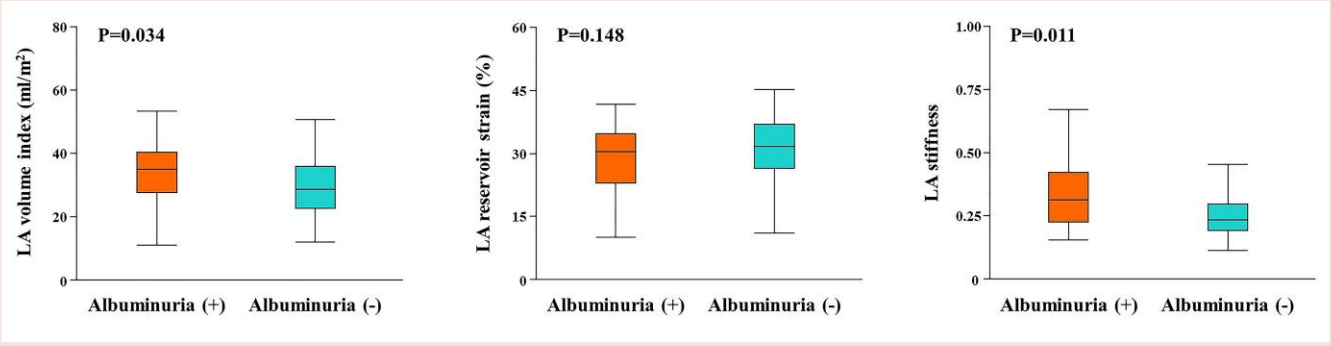


Figure 3 LA structure and function in albuminuria group and non-albuminuria group after CA. CA, catheter ablation; LA, left atrium.

subsequent cardiovascular disease.[29,30] Of note, patients with albuminuria had similar eGFR values compared with those without albuminuria in our study, highlighting the importance of evaluating the UACR in AF patients with preserved or mildly reduced eGFR.

Study strength and limitations

The strengths of this study include the comprehensive evaluation of LA morphology and function by STE before and after CA in AF patients with preserved or mildly reduced eGFR. Several limitations should be noted. First, the evaluation of albuminuria was only once in the present study, which may be insufficient for obtaining an accurate assessment because the level of albuminuria would be dynamic based on hydration status and exercise. However, the initial assessment of albuminuria using a single urine sample reflects current clinical practice, and relatively high agreement between UACR and 24-h urinary albumin excretion was reported.[31] Second, we cannot confirm a cause-effect relationship between albuminuria and LA remodelling due to the observational nature of the present study. Third, we included patients who underwent CA, which may limit the applicability of the findings to other populations with different conditions, such as patients with long-standing AF who are ineligible for CA therapy. Fourth, although we accounted for several potential confounders and performed multivariable analyses adjusting for AF risk factors, laboratory parameters, and echocardiographic measures, we cannot rule out the potential reverse causality and possibility of unmeasured factors which could play a role in our observation. Finally, the study period was relatively short, and we could not determine if patients with albuminuria have poor outcomes such as recurrent AF as well as stroke and heart failure.

Conclusions

Albuminuria was observed in 16% of AF patients with preserved or mildly reduced eGFR who underwent CA. Patients with albuminuria had more advanced LA remodelling than patients without albuminuria, and the association persisted after CA. Our findings may indicate that close follow-up after CA is warranted in patients with albuminuria.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Disclosure statement

All authors report no disclosures pertinent to the content of the manuscript.

Authors' contribution

K.N. contributed to the conception and design of the work. K.N., M.D., K.F., K.I., K.H., Y.Yo., Y.M., H.S., Y.Ya., M.H., T.N., T.O., T.M., Y.S., G.O., T.K., and E.H. contributed to the acquisition, analysis, and interpretation

of the data for the study. K.N. drafted the manuscript. M.D., K.F., K.I., K.H., Y.Yo., Y.M., H.S., Y.Ya., M.H., T.N., T.O., T.M., Y.S., G.O., T.K., E.H., H.M., M.K., and N.T. critically revised the manuscript. All authors provided final approval and agreed to be accountable for all aspects of the work, ensuring integrity and accuracy.

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