

Original Article



Clinical and Imaging Parameters Associated With Impaired Kidney Function in Patients With Acute Decompensated Heart Failure With Reduced Ejection Fraction

In-Jeong Cho , MD, PhD, Sang-Eun Lee , MD, PhD, Dong-Hyeok Kim , MD, and Wook Bum Pyun , MD, PhD

Division of Cardiology, Department of Internal Medicine, Ewha Womans University Seoul Hospital, Ewha Womans University College of Medicine, Seoul, Korea



Received: Jan 5, 2023
Revised: Feb 16, 2023
Accepted: Mar 19, 2023
Published online: Mar 29, 2023

Address for Correspondence:

In-Jeong Cho, MD, PhD
Division of Cardiology, Department of Internal Medicine, Ewha Womans University College of Medicine, 260 Gonghang-daero, Gangseo-gu, Seoul 07804, Korea.
Email: icho@ewha.ac.kr

Copyright © 2023 Korean Society of Echocardiography

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

BACKGROUND: Acute worsening of cardiac function frequently leads to kidney dysfunction. This study aimed to identify clinical and imaging parameters associated with impaired kidney function in patients with acute decompensated heart failure with reduced ejection fraction (HFrEF).

METHODS: Data from 131 patients hospitalized with acute decompensated HFrEF (left ventricular ejection fraction, < 40%) were analyzed. Patients were divided into two groups according to the glomerular filtration rate (GFR) at admission (those with preserved kidney function [GFR \geq 60 mL/min/1.73 m²] and those with reduced kidney function [GFR < 60 mL/min/1.73 m²]). Various echocardiographic parameters and perirenal fat thicknesses were assessed by computed tomography.

RESULTS: There were 71 patients with preserved kidney function and 60 patients with reduced kidney function. Increased age (odds ratio [OR], 1.07; 95% confidence interval [CI], 1.04–1.12; $p = 0.005$), increased log N-terminal pro b-type natriuretic peptide (OR, 1.74; 95% CI, 1.14–2.66; $p = 0.010$), and increased perirenal fat thickness (OR, 1.19; 95% CI, 1.10–1.29; $p < 0.001$) were independently associated with reduced kidney function, even after adjusting for variable clinical and echocardiographic parameters. The optimal average perirenal fat thickness cut-off value of > 12 mm had a sensitivity of 55% and specificity of 83% for kidney dysfunction prediction.

CONCLUSIONS: Thick perirenal fat was independently associated with impaired kidney function in patients hospitalized for acute decompensated HFrEF. Measurement of perirenal fat thickness may be a promising imaging marker for the detection of HFrEF patients who are more susceptible to kidney dysfunction.

Keywords: Heart failure; Kidney; Adipose tissue

INTRODUCTION

Acute decompensated heart failure is one of the leading causes of hospitalization in the elderly population.¹⁾ More than 70% of patients, who were hospitalized for acute decompensated heart failure, experienced acute deterioration of kidney function, which was associated with high mortality and readmission rates.^{2,3)} Kidney dysfunction in heart failure with reduced ejection fraction (HFrEF) has traditionally been considered to result from decreased perfusion to the kidney associated with impairment of cardiac output or intravascular volume depletion.⁴⁾ However, renal venous congestion has recently been regarded as a more important determinant for the development of kidney dysfunction in heart failure.⁵⁻⁷⁾

The kidney is surrounded by a rigid and non-expandable fascia in the perirenal space.⁸⁾ The perirenal space consists mainly of adipose tissue and additional renal vasculature, lymphatic system, and adrenal gland. The thickness of the perirenal fat around the kidney and renal sinus adipose tissue are reportedly associated with various chronic and metabolic diseases, such as chronic kidney disease, arteriosclerosis, hypertension, and diabetes.^{9,11)} In heart failure patients with congestion, increased volume of adipose tissue within the perirenal space may accelerate the increase in perirenal pressure due to limited space surrounded by non-expandable fascia.¹²⁾ Recently, perirenal fat has been shown to play a role in acute kidney function deterioration in patients with acute decompensated heart failure by compressing the renal vasculature, leading to pathologic activation of the renin-angiotensin-aldosterone system and reduced renal perfusion,¹²⁾ suggesting an association of perirenal adipose tissue amount with kidney dysfunction in patients with heart failure.

The current study aimed to assess the clinical and imaging parameters associated with kidney dysfunction in patients with acute decompensated HFrEF, and to identify patients who are susceptible to kidney dysfunction in this population. For this purpose, various echocardiographic variables and perirenal fat thickness were assessed to identify factors associated with kidney dysfunction in patients with acute decompensated HFrEF.

METHODS

Study population

This retrospective cohort study used electronic medical records and imaging data. We analyzed the data of patients hospitalized for acute decompensated HFrEF between February 2019 and May 2022 at a single center for cardiovascular disease in

Korea. HFrEF was defined as heart failure with left ventricular (LV) ejection fraction (EF) < 40%.¹³⁾ The exclusion criteria were as follows: acute myocardial infarction, aborted sudden cardiac death, hypertrophic cardiomyopathy, peripartum cardiomyopathy, active infective endocarditis, significant organic valvular heart diseases, prosthetic heart valves, isolated right ventricular failure, single kidney, history of kidney transplantation, and known chronic kidney disease, defined as glomerular filtration rate (GFR) < 60 mL/min/1.73 m² for 3 months or more prior to the index admission. Those without computed tomography (CT) data covering fields at the kidney level within 6 months of index admission were also excluded. A total of 131 patients hospitalized with acute decompensated HFrEF were included in the final analysis. Patients were divided into two groups according to the GFR at admission: preserved kidney function (GFR ≥ 60 mL/min/1.73 m²) and reduced kidney function (GFR < 60 mL/min/1.73 m²). Patients with reduced kidney function were further divided into two groups according to the peak GFR during hospitalization: recovered kidney dysfunction (peak GFR ≥ 60 mL/min/1.73 m²) and persistent kidney dysfunction (peak GFR < 60 mL/min/1.73 m²).

This study was approved by the ethics committee of our institution (institutional review board number: SEUMC 2022-06-036). The need for informed consent from patients was waived owing to the retrospective nature of the study.

Clinical variables

Data regarding the presence of hypertension, diabetes mellitus, coronary artery disease, and atrial fibrillation were retrieved from medical records. Height, weight, and blood pressure (BP) were measured during admission, and the first value after admission was used in the analysis. Body mass index (BMI) was calculated using height and weight.

Laboratory tests, including creatinine and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels, were performed at admission. Kidney function was defined by GFR, calculated using the formula developed and validated in the Modification of Diet in Renal Disease study as follows¹⁴⁾: $GFR (mL/min/1.73 m^2) = 186.3 \times (\text{serum creatinine [mg/dL]}^{-1.154} \times \text{age}^{-0.203} (\times 0.742, \text{ for female}))$. NT-proBNP levels were logarithmically transformed to achieve a normal distribution.

Imaging modalities

Data from the first transthoracic echocardiography after index admission were used in the analysis. The LV end-diastolic dimension (EDD) and end-systolic dimension (ESD) were measured from two-dimensional echocardiographic images. LV

EF was calculated using the LV end-diastolic and end-systolic volumes. LV mass was calculated using a formula proposed by the American Society of Echocardiography guidelines.¹⁵ The LV mass index was defined as the LV mass divided by the body surface area. Left atrial volume was calculated using the biplane method of disks, in which two-dimensional volumetric measurements were based on left atrial area measurements using tracings of the blood-tissue interface on apical four- and two-chamber views.¹⁵ Left atrial volume index (LAVI) was defined as the left atrial volume divided by the body surface area.

The mitral inflow velocities were obtained from the apical four-chamber view. The mitral peak early diastolic (E) velocity and peak early diastolic mitral annular velocity (e') were measured. We calculated the E/e' ratio by dividing the E velocity by the e' velocity. Stroke volume was calculated using LV outflow tract diameter and pulse-wave Doppler. The stroke volume index was defined as the stroke volume indexed for the body surface area. The calculated systolic pulmonary artery pressure (SPAP) was defined as $4 \times (\text{peak velocity of tricuspid regurgitation [TR] jet})^2 + \text{right atrial (RA) pressure}$. RA pressure was estimated by measuring the inferior vena cava (IVC) diameter and associated respiratory changes. The IVC diameter was measured perpendicular to the long axis of the IVC at end-expiration, just proximal to the junction of the hepatic veins that lie approximately 0.5 to 3.0 cm proximal to the ostium of the right atrium (**Figure 1A**). IVC diameter ≤ 2.1 cm that collapses $> 50\%$ with inspiration suggests a normal RA pressure of 3 mmHg, whereas an IVC diameter > 2.1 cm that collapses $< 50\%$ with inspiration suggests an RA pressure of 15 mmHg. In scenarios in which IVC diameter and collapse did not fit this paradigm,

an intermediate value of 8 mmHg was used, according to the American Society of Echocardiography guidelines.¹⁶

CT images were used for perirenal fat thickness analysis. The posterior perirenal fat thickness was measured (**Figure 1B**). Perirenal fat thickness was defined as the direct distance from the posterior capsule to the posterior abdominal wall at the level of the renal vein.¹⁷ The average value of perirenal fat was calculated using the right and left posterior perirenal fat thicknesses.

Statistical analysis

Demographic characteristics were reported as percentages or means \pm standard deviations. The patient groups were compared using χ^2 statistics for categorical variables and the Student's t-test for continuous variables. Correlation between the variables was assessed with the Pearson correlation test. To determine potential independent associations between variables and reduced kidney function, binary logistic regression was applied. Variables with p values < 0.2 in the univariate analysis were entered into the multivariate binary logistic regression model, and the odds ratio (OR) and 95% confidence interval (CI) were reported. Linear logistic regression was applied to determine the potential independent correlation between the variables and perirenal fat thickness. Variables displaying a p value < 0.2 in univariate analysis were entered into the multivariate linear logistic regression model. Receiver operating characteristic curves were plotted to determine the sensitivity and specificity of different perirenal fat thicknesses for kidney dysfunction prediction and to determine the cut-off value. Statistical significance was set at $p < 0.05$.

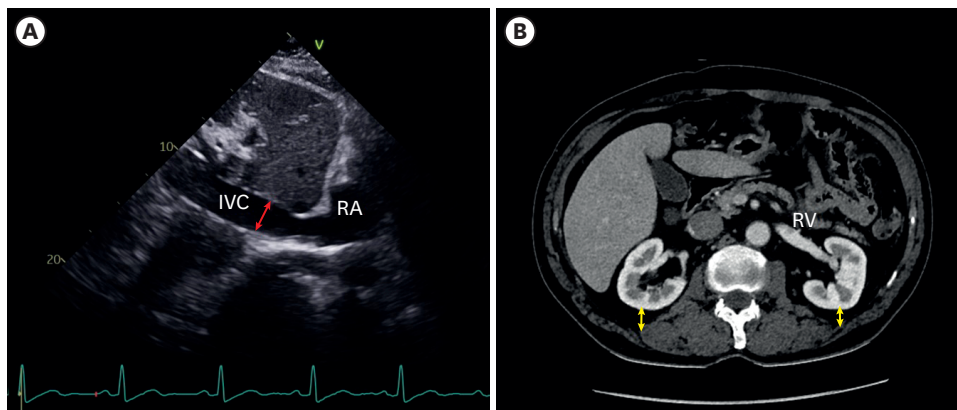


Figure 1. (A) Inferior vena cava measurement by echocardiography and (B) Perirenal fat thickness measurement by computed tomography. A red double-headed arrow indicates inferior vena cava diameter. Yellow double-headed arrows indicate the posterior perirenal fat thickness. IVC: inferior vena cava, RA: right atrium, RV: renal vein.

RESULTS

Patient characteristics

Among the 131 patients hospitalized with acute decompensated HFrEF, 112 (85.5%) were first diagnosed with heart failure and 19 (14.5%) had acute exaggeration of previously diagnosed heart failure. There were 71 patients with preserved kidney function and 60 patients with reduced kidney function. The mean GFR was 81.9 ± 15.2 mL/min/1.73 m² and 40.1 ± 10.6 mL/min/1.73 m² in the preserved and reduced kidney function groups, respectively.

Table 1 showed the baseline characteristics of the study population. Patients with reduced kidney function were older than those with preserved kidney function (81 ± 8 vs. 71 ± 15 years, $p < 0.001$). There were no significant differences in the prevalence of women, hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, BMI, systolic BP, or diastolic BP between patients with preserved kidney function and those

with reduced kidney function. Echocardiographic variables, including LV EDD, LV ESD, LV EF, LV mass index, LAVI, E/e', peak TR velocity, RA pressure, SPAP, and cardiac index, were comparable between two groups. Among the echocardiographic variables, the only factor with a significant difference between two groups was stroke volume index, which was higher in patients with reduced kidney function (30.9 ± 12.1 mL/m² vs. 26.6 ± 9.7 mL/m², $p = 0.024$). Log NT-proBNP (9.4 ± 1.1 pg/mL vs. 8.7 ± 1.0 pg/mL, $p < 0.001$) and average perirenal fat thickness (13.5 ± 9.8 mm vs. 7.2 ± 4.8 mm, $p < 0.001$) were all higher in those with reduced kidney function compared to those with preserved kidney function.

Associated factors with reduced kidney function

There was significant negative correlation between average perirenal fat thickness and GFR ($r = -0.448$, $p < 0.001$). **Figure 2** demonstrates the spline curve showing the correlation between average perirenal fat thickness and GFR.

Table 1. Baseline characteristics of the study population

Variables	Overall (n = 131)	Kidney function at admission		p-value
		Preserved kidney function (n = 71)	Reduced kidney function (n = 60)	
Demographics				
Age (years)	76 ± 13	71 ± 15	81 ± 8	< 0.001*
Female sex	74 (56.5)	38 (53.5)	36 (60.0)	0.456
Hypertension	43 (32.8)	25 (35.2)	18 (30.0)	0.527
Diabetes mellitus	31 (23.7)	13 (18.3)	18 (30.0)	0.117
Coronary artery disease	31 (23.7)	16 (22.5)	15 (25.0)	0.741
Atrial fibrillation	45 (34.4)	25 (35.2)	20 (33.3)	0.822
Body mass index (kg/m ²)	23.1 ± 4.9	22.8 ± 5.1	23.4 ± 4.8	0.539
Systolic BP (mmHg)	131.2 ± 19.8	128.2 ± 20.0	134.6 ± 19.2	0.066
Diastolic BP (mmHg)	76.6 ± 15.1	77.9 ± 16.6	75.2 ± 13.1	0.311
Echocardiography				
LV EDD (mm)	58.5 ± 7.5	58.9 ± 8.3	58.3 ± 6.5	0.845
LV ESD (mm)	49.9 ± 8.5	50.2 ± 9.5	49.6 ± 7.2	0.698
LV EF (%)	25.8 ± 8.2	25.2 ± 8.9	26.5 ± 7.3	0.354
LV mass index (g/m ²)	144.9 ± 40.8	140.4 ± 37.8	150.2 ± 43.9	0.174
LAVI (mL/m ²)	59.3 ± 18.3	58.7 ± 18.0	60.0 ± 18.8	0.703
E/e'	22.2 ± 10.2	21.8 ± 10.0	22.5 ± 10.4	0.697
Peak TR velocity (m/s)	2.7 ± 0.5	2.7 ± 0.5	2.8 ± 0.5	0.794
RA pressure (mmHg)	7.8 ± 5.5	7.8 ± 5.9	7.8 ± 5.0	0.926
SPAP (mmHg)	39.3 ± 14.5	38.6 ± 14.6	40.1 ± 14.5	0.584
Stroke volume index (mL/m ²)	28.5 ± 11.0	26.6 ± 9.7	30.9 ± 12.1	0.024*
Cardiac index (L/min/m ²)	2.5 ± 0.9	2.4 ± 0.9	2.6 ± 1.0	0.225
Laboratory findings				
GFR (mL/min/1.73 m ²)	62.8 ± 24.7	81.9 ± 15.2	40.1 ± 10.6	< 0.001*
Log NT-proBNP (pg/mL)	9.0 ± 1.1	8.7 ± 1.0	9.4 ± 1.1	< 0.001*
Computed tomography				
Right perirenal fat thickness (mm)	9.9 ± 8.2	6.8 ± 4.9	13.5 ± 9.8	< 0.001*
Left perirenal fat thickness (mm)	10.5 ± 8.2	7.2 ± 5.2	14.4 ± 9.2	< 0.001*
Average perirenal fat thickness (mm)	10.1 ± 7.6	7.2 ± 4.8	13.5 ± 8.8	< 0.001*

BP: blood pressure, E/e': the ratio of early diastolic mitral inflow to mitral annular velocity, EDD: end-diastolic dimension, EF: ejection fraction, ESD: end-systolic dimension, GFR: glomerular filtration rate, LAVI: left atrial volume index, LV: left ventricular, NT-proBNP: N-terminal pro b-type natriuretic peptide, RA: right atrial, SPAP: systolic pulmonary artery pressure, TR: tricuspid regurgitation.

*p-value < 0.05.

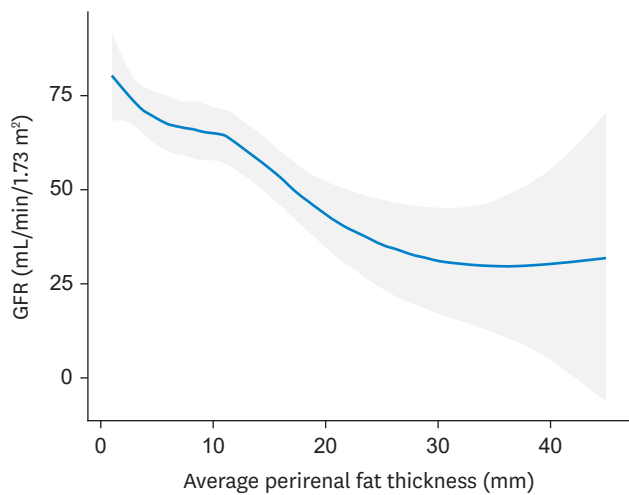


Figure 2. Spline curve in the correlation between average perirenal fat thickness and GFR. Shadow area is the 95% confidence interval of the predicted GFR (solid blue line). GFR: glomerular filtration rate.

Table 2 showed the univariate and multivariate logistic regression analyses for factors associated with reduced kidney function. In the univariate analysis, age (OR, 1.07; 95% CI, 1.03–1.11, $p < 0.001$), stroke volume index (OR, 1.04; 95% CI, 1.00–1.07; $p = 0.028$), log NT-proBNP (OR, 1.83; 95% CI, 1.29–2.61; $p = 0.001$), and average perirenal fat thickness (OR, 1.16;

95% CI, 1.08–1.24; $p < 0.001$) were significantly associated with reduced kidney function. In the multivariate analysis, increasing age (OR, 1.07; 95% CI, 1.04–1.12; $p = 0.005$), increased log NT-proBNP (OR, 1.74; 95% CI, 1.14–2.66; $p = 0.010$), and increasing average perirenal fat thickness (OR: 1.19, 95% CI: 1.10–1.29, $p < 0.001$) were independently associated with reduced kidney function, even after adjusting for diabetes mellitus, systolic BP, LV mass index, and stroke volume index.

The receiver operating characteristic curve analysis for the prediction of kidney dysfunction using the average perirenal fat thickness demonstrated an area under the curve of 0.729 (95% CI, 0.642–0.816; $p < 0.001$). The optimal average perirenal fat thickness cut-off value of > 12 mm had a sensitivity of 55% and specificity of 83% for the prediction of kidney dysfunction.

Correlated factors with perirenal fat thickness

The clinical characteristics correlated with the average perirenal fat thickness were shown in **Table 3**. In the univariate analysis, BMI, systolic BP, and coronary artery disease were positively correlated with perirenal fat thickness. However, factors showing an independent correlation with increasing perirenal fat thickness were increasing BMI ($p < 0.001$) and the presence of coronary artery disease ($p = 0.033$) in the multivariate analysis.

Table 2. Factors associated with kidney dysfunction in patients with acute heart failure and reduced ejection fraction

Variables	Univariable			Multivariable		
	OR	95% CI	p-value	OR	95% CI	p-value
Age, per year	1.07	1.03–1.11	$< 0.001^*$	1.07	1.02–1.12	0.005*
Female sex	1.30	0.65–2.61	0.456	-	-	-
Hypertension	0.79	0.38–1.65	0.527	-	-	-
Diabetes mellitus	1.91	1.85–4.33	0.120	2.22	0.82–6.14	0.124
Coronary artery disease	1.15	0.51–2.57	0.741	-	-	-
Atrial fibrillation	0.92	0.45–1.90	0.822	-	-	-
Body mass index	1.02	0.95–1.10	0.537	-	-	-
Systolic BP	1.02	1.00–1.04	0.069	1.00	0.97–1.02	0.390
Diastolic BP	0.99	0.97–1.01	0.309	-	-	-
LV EDD	1.00	0.95–1.04	0.843	-	-	-
LV ESD	0.99	0.95–1.03	0.696	-	-	-
LV EF	1.02	0.98–1.07	0.351	-	-	-
LV mass index	1.01	1.00–1.02	0.177	1.00	0.99–1.02	0.390
LAVI	1.00	0.99–1.02	0.701	-	-	-
E/e'	1.01	0.97–1.04	0.695	-	-	-
RA pressure	1.00	0.94–1.07	0.926	-	-	-
SPAP	1.01	0.98–1.03	0.581	-	-	-
Stroke volume index	1.04	1.00–1.07	0.028*	1.03	0.98–1.09	0.241
Cardiac index	1.23	0.87–1.83	0.224	-	-	-
Log NT-proBNP	1.83	1.29–2.61	0.001*	1.74	1.14–2.66	0.010*
Average perirenal fat thickness	1.16	1.08–1.24	$< 0.001^*$	1.19	1.10–1.29	$< 0.001^*$

BP: blood pressure, CI: confidence interval, E/e': the ratio of early diastolic mitral inflow to mitral annular velocity, EDD: end-diastolic dimension, EF: ejection fraction, ESD: end-systolic dimension, LAVI: left atrial volume index, LV: left ventricular, NT-proBNP: N-terminal pro b-type natriuretic peptide, OR: odds ratio, RA: right atrial, SPAP: systolic pulmonary artery pressure.

*p-value < 0.05 .

Kidney Dysfunction in HFrEF

Table 3. Clinical characteristics correlated with perirenal fat thickness

Variables	Univariable			Multivariable		
	beta	t	p-value	beta	t	p-value
Age	0.11	1.25	0.214	-	-	-
Female sex	-0.01	-1.11	0.268	-	-	-
Hypertension	-0.02	-0.25	0.805	-	-	-
Diabetes mellitus	0.08	0.86	0.394	-	-	-
Coronary artery disease	0.15	1.74	0.084	0.18	2.15	0.033*
Atrial fibrillation	-0.6	0.66	0.513	-	-	-
Body mass index	0.30	3.28	< 0.001*	0.29	3.36	0.001*
Systolic BP	0.21	2.44	0.016*	0.14	1.61	0.110
Diastolic BP	0.07	8.15	0.417	-	-	-

BP: blood pressure.

*p-value < 0.05.

Comparison between recovered and persistent kidney dysfunction

There were 30 patients with recovered kidney dysfunction and 30 patients with persistent kidney function during the hospitalization period among the 60 patients who initially presented with kidney dysfunction. Follow-up peak GFR was 79.9 ± 16.0 mL/min/1.73 m² in those with recovered kidney dysfunction and 44.8 ± 9.0 mL/min/1.73 m² in those with persistent kidney dysfunction, respectively.

The characteristics of the patients with recovered kidney dysfunction and persistent kidney dysfunction were shown in the Supplementary Table. There were no significant differences in age, sex, prevalence of hypertension, diabetes mellitus, coronary artery disease, BMI, systolic BP, or diastolic BP between those with recovered and persistent kidney dysfunction. Echocardiographic variables, including LV EDD, LV

ESD, LV EF, LV mass index, LAVI, E/e', peak TR velocity, SPAP, stroke volume index, and cardiac index, were all comparable between two groups. However, RA pressure (9.5 ± 5.4 mmHg vs. 6.1 ± 3.9 mmHg, $p = 0.009$) was significantly higher in patients with recovered kidney dysfunction than in those with persistent kidney dysfunction (**Figure 3A**). While there were no significant differences in the average perirenal fat thickness (12.9 ± 8.2 mm vs. 14.0 ± 10.6 mm, $p = 0.625$) between two groups, perirenal fat thickness was higher in both groups than in those with preserved kidney function (all $p < 0.05$) (**Figure 3B**).

DISCUSSION

The principal findings of the current study were that 1) factors independently associated with kidney dysfunction were increasing age, high NT-proBNP, and increasing perirenal fat thickness; 2) average perirenal fat thickness > 12 mm had a high specificity for prediction of kidney dysfunction in acute decompensated HFrEF; and 3) distinct features of patients with transient kidney dysfunction at initial presentation of heart failure were high RA pressure and thick perirenal fat in patients with HFrEF.

Factors associated with kidney dysfunction in acute decompensated heart failure

Our study demonstrated concordant results with the previous data, showing that factors associated with renal congestion were more hemodynamically important than the impairment of cardiac output for the development of kidney dysfunction.⁵⁷⁾ In the

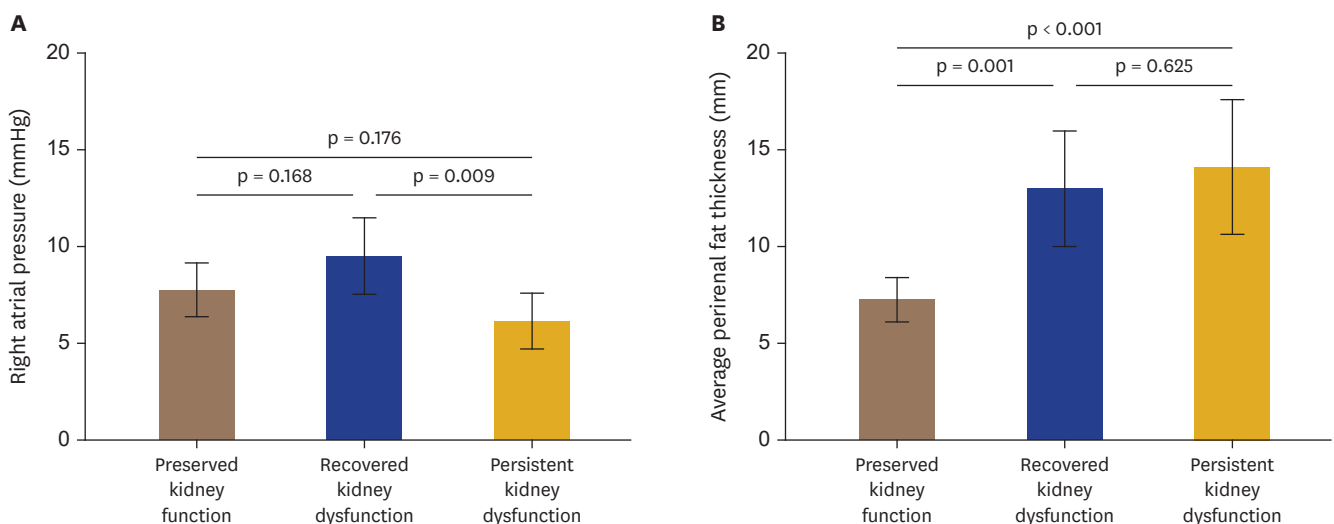


Figure 3. Comparisons of right atrial pressure and average perirenal fat thickness between those with preserved kidney function, recovered kidney dysfunction, and persistent kidney dysfunction. (A) Right atrial pressure and (B) Average perirenal fat thickness. Error bars indicate 2 standard errors of the mean.

current study, stroke volume index, which reflects cardiac output, was not reduced in patients with kidney dysfunction, while log NT-proBNP and perirenal fat thickness showed a significant independent association with reduced kidney function. An average perirenal fat thickness of > 12 mm had a high specificity for predicting kidney dysfunction in acute decompensated HFrEF, suggesting that patients with perirenal fat thickness < 12 mm might have a low probability of kidney dysfunction at the time of acute decompensated heart failure status.

The perirenal fat pad has been suggested to play a role in decline in kidney function in patients with heart failure by compressing the renal vasculature, leading to activation of the renin-angiotensin-aldosterone system.¹²⁾ Both the thickness of the perirenal fat tissue surrounding the kidney and accumulation of fat in the renal sinus have been associated with chronic kidney disease, arteriosclerosis, hypertension, and diabetes.^{9,11)} The perirenal space consists mainly of adipose tissue, and an increase in adipose tissue volume within the perirenal space in non-expandable fascia may lead to increased perirenal pressure when systemic congestion occurs in heart failure. In studies with animal models of heart failure and acute renal ischemia, renal decapsulation has been shown effective in alleviating pressure-related injury within the kidney,¹²⁾ which supports the pivotal role of perirenal fat and its compressive effect on the development of kidney dysfunction in patients with systemic congestion due to acute exaggeration of heart failure.¹⁸⁾

Elevated RA pressure reflects systemic congestion. The RA pressure can be assessed with echocardiography by measuring IVC diameter. Previous studies showed that increased IVC diameter was associated with adverse outcomes in heart failure.¹⁹⁾ Interestingly, we found that the distinct feature of patients with transient kidney dysfunction at admission for acute decompensated heart failure was elevated RA pressure. High RA pressure, a sign of right-sided congestion, is likely to be associated with renal congestion and may adversely affect the kidney function. We found that HFrEF patients with high RA pressure demonstrated better kidney outcomes compared with those with low RA pressure during hospitalization of heart failure. We can speculate that those with high RA pressure and thick perirenal fat have the higher burden of renal compression caused by systemic and perirenal congestion, which can be alleviated effectively by diuretics therapy, and have the higher chance of functional recovery in kidney dysfunction. However, patients with kidney dysfunction and low RA pressure have the lower chance of kidney functional recovery, since acute systemic congestion may not be the main cause of the development of kidney dysfunction.

Taken together, we can speculate that patients with HFrEF with thin perirenal fat (thickness < 12 mm) have a low probability of renal dysfunction in a state of acute decompensation. HFrEF patients with thick perirenal fat have a higher probability of kidney dysfunction, while those with high RA pressure and thick perirenal fat have a high probability of recovery from kidney dysfunction if timely and appropriate diuresis is provided at the presentation of acute decompensated heart failure. A subgroup of patients with HFrEF with low LA pressure and thick perirenal fat may have a low chance of recovery from kidney dysfunction.

Factors related with perirenal fat thickness

While perirenal fat shares the same developmental origin as typical visceral fat, these adipose tissue depots differ in terms of histology, physiology, and functions.¹⁰⁾ Perirenal fat has been recently recognized as an important factor that contributes to the maintenance of the cardiovascular system and kidney homeostasis.⁸⁾ A direct correlation between perirenal fat thickness and kidney damage has been reported; however,¹¹⁾ the mechanism of perirenal fat involvement in chronic kidney damage is not completely clarified. In this regard, increased perirenal fat may result in direct compression and obstruction of renal parenchyma and vessels, followed by an increase in sodium reabsorption with alterations of renal functions.²⁰⁾

CT is a reliable and useful tool to quantify adipose tissues. Among visceral adipose tissue depots, perirenal fat, which is located in the retroperitoneal space and surrounds the kidneys, can be easily measured using CT. The perirenal fat thickness at the level of the renal vein measured by CT scan showed a good positive correlation with whole perirenal fat mass,²¹⁾ suggesting that perirenal fat thickness can be a good estimate of the individual's perirenal adipose tissue burden in the perirenal space.

We found that factors showing an independent correlation with posterior perirenal fat thickness were increasing BMI and the presence of coronary artery disease. Visceral adiposity was associated with a greater risk of cardiorenal morbidity than subcutaneous adiposity.²²⁾ Perirenal fat has been reported as an indirect measurement that correlated with visceral fat,^{9,23)} and the evaluation of perirenal fat volume has been proposed as a parameter for the assessment of early renal lesions associated with obesity.²⁴⁾ Furthermore, perirenal fat would be a promising target for kidney dysfunction in heart failure, and some authors even recommended renal decapsulation as a potentially interesting novel treatment for heart failure and acute renal ischemia due to congestion.¹²⁾ In this aspect, it would be worthwhile to investigate whether weight reduction in obese

patients could decrease visceral and perirenal fat, followed by reducing the risk of kidney dysfunction in patients with HFrEF. Further studies on the relationship between obesity, visceral fat, perirenal fat, and HFrEF are warranted.

Limitations

The main limitation of the current study was that the results were based on a retrospective data analysis. However, the patients' medical records and echocardiographic and CT images were carefully reviewed to minimize bias. Second, the perirenal fat thickness was measured in a single plane in the posterior direction, while the perirenal fat was located around the kidney. Therefore, studies using multidirectional or volumetric measurements are warranted for a more accurate measurement of perirenal fat. However, perirenal fat thickness measured using CT at the level of the renal veins has been reported to be a simple and reliable estimate of perirenal fat volume,²¹⁾ and our simple measurement method would be more useful and easy to apply in clinical practice. Third, we assumed RA pressure only by measuring the IVC diameter, even though the guideline recommended consideration of other parameters in scenarios in which IVC diameter and collapse did not fit the normal or high RA pressure criteria.¹⁶⁾ Fourth, the current study has a cross-sectional design, which limits its ability to investigate the association between perirenal fat thickness and the prognosis of patients with HFrEF. Fifth, since perirenal fat thickness varies depending on body weight, an indexed value may be a more accurate parameter for assessing renal risk. Further studies are needed to compare perirenal fat thickness and its indexed value to determine which is more clinically useful. Finally, although the stroke volume index was higher in the reduced kidney function group, LV EDD, LV EF, and cardiac index were not different between the two groups. It remains to be determined through studies with larger patient populations whether these results are clinically significant or merely coincidental.

CONCLUSION

A thick perirenal fat pad was independently associated with kidney dysfunction in patients hospitalized with acute decompensated HFrEF. Measurement of perirenal fat thickness may be a promising imaging marker for the detection of HFrEF patients who are more susceptible to kidney dysfunction. Distinct features of HFrEF patients with transient kidney dysfunction at the time of heart failure presentation were high RA pressure and thick perirenal fat pads.

ORCID iDs

In-Jeong Cho 
<https://orcid.org/0000-0002-1209-5129>
 Sang-Eun Lee 
<https://orcid.org/0000-0001-6645-4038>
 Dong-Hyeok Kim 
<https://orcid.org/0000-0002-6339-8496>
 Wook Bum Pyun 
<https://orcid.org/0000-0002-6377-0411>

Funding

This study was supported by a research grant of the Korean Society of Echocardiography (2017).

Conflict of Interest

The authors have no financial conflicts of interest.

Author Contributions

Conceptualization: Cho IJ; Data curation: Lee SE, Kim DH; Formal analysis: Cho IJ; Funding acquisition: Cho IJ; Writing - original draft: Cho IJ; Writing - review & editing: Lee SE, Kim DH, Pyun WB.

REFERENCES

- Jiang HJ, Russo CA, Barrett ML. Nationwide Frequency and Costs of Potentially Preventable Hospitalizations, 2006. Rockville, MD: Agency for Healthcare Research and Quality (US); 2006.
- Jong P, Vowinkel E, Liu PP, Gong Y, Tu JV. Prognosis and determinants of survival in patients newly hospitalized for heart failure: a population-based study. *Arch Intern Med* 2002;162:1689-94.
[PUBMED](#) | [CROSSREF](#)
- Hernandez AF, Greiner MA, Fonarow GC, et al. Relationship between early physician follow-up and 30-day readmission among Medicare beneficiaries hospitalized for heart failure. *JAMA* 2010;303:1716-22.
[PUBMED](#) | [CROSSREF](#)
- Ljungman S, Laragh JH, Cody RJ. Role of the kidney in congestive heart failure. Relationship of cardiac index to kidney function. *Drugs* 1990;39 Suppl 4:10-21.
[PUBMED](#) | [CROSSREF](#)
- Mullens W, Abrahams Z, Francis GS, et al. Importance of venous congestion for worsening of renal function in advanced decompensated heart failure. *J Am Coll Cardiol* 2009;53:589-96.
[PUBMED](#) | [CROSSREF](#)
- Damman K, van Deursen VM, Navis G, Voors AA, van Veldhuisen DJ, Hillege HL. Increased central venous pressure is associated with impaired renal function and mortality in a broad spectrum of patients with cardiovascular disease. *J Am Coll Cardiol* 2009;53:582-8.
[PUBMED](#) | [CROSSREF](#)
- Husain-Syed F, Gröne HJ, Assmus B, et al. Congestive nephropathy: a neglected entity? Proposal for diagnostic criteria and future perspectives. *ESC Heart Fail* 2021;8:183-203.
[PUBMED](#) | [CROSSREF](#)
- Grigoraş A, Balan RA, Căruntu ID, et al. Perirenal adipose tissue-current knowledge and future opportunities. *J Clin Med* 2021;10:1291.
[PUBMED](#) | [CROSSREF](#)
- Geraci G, Zammuto MM, Mattina A, et al. Para-perirenal distribution of body fat is associated with reduced glomerular filtration rate regardless of other indices of adiposity in hypertensive patients. *J Clin*

- Hypertens (Greenwich)* 2018;20:1438-46.
[PUBMED](#) | [CROSSREF](#)
10. Liu BX, Sun W, Kong XQ. Perirenal fat: a unique fat pad and potential target for cardiovascular disease. *Angiology* 2019;70:584-93.
[PUBMED](#) | [CROSSREF](#)
 11. D'Marco L, Salazar J, Cortez M, et al. Perirenal fat thickness is associated with metabolic risk factors in patients with chronic kidney disease. *Kidney Res Clin Pract* 2019;38:365-72.
[PUBMED](#) | [CROSSREF](#)
 12. Boorsma EM, Ter Maaten JM, Voors AA, van Veldhuisen DJ. Renal compression in heart failure: the renal tamponade hypothesis. *JACC Heart Fail* 2022;10:175-83.
[PUBMED](#) | [CROSSREF](#)
 13. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2022;145:e895-1032.
[PUBMED](#) | [CROSSREF](#)
 14. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med* 2003;139:137-47.
[PUBMED](#) | [CROSSREF](#)
 15. Lang RM, Badano LP, Mor-Avi V, 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. *J Am Soc Echocardiogr* 2015;28:1-39.e14.
[PUBMED](#) | [CROSSREF](#)
 16. Rudski LG, Lai WW, Afilalo J, 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;23:685-713.
[PUBMED](#) | [CROSSREF](#)
 17. Yao Y, Gong H, Pang Y, et al. Risk factors influencing the thickness and stranding of perinephric fat of mayo adhesive probability score in minimally invasive nephrectomy. *Med Sci Monit* 2019;25:3825-31.
[PUBMED](#) | [CROSSREF](#)
 18. Cho JJ, Wi J, Lee SE, Kim DH, Pyun WB. Perirenal fat and kidney function deterioration in patients with acute decompensated heart failure. *Int J Heart Fail* 2023;5:36-47.
[PUBMED](#) | [CROSSREF](#)
 19. Abe H, Kosugi S, Ozaki T, et al. Prognostic impact of echocardiographic congestion grade in HFpEF with and without atrial fibrillation. *JACC Asia* 2022;2:73-84.
[PUBMED](#) | [CROSSREF](#)
 20. Huang N, Mao EW, Hou NN, Liu YP, Han F, Sun XD. Novel insight into perirenal adipose tissue: a neglected adipose depot linking cardiovascular and chronic kidney disease. *World J Diabetes* 2020;11:115-25.
[PUBMED](#) | [CROSSREF](#)
 21. Favre G, Grangeon-Chapon C, Raffaelli C, François-Chalmin F, Iannelli A, Esnault V. Perirenal fat thickness measured with computed tomography is a reliable estimate of perirenal fat mass. *PLoS One* 2017;12:e0175561.
[PUBMED](#) | [CROSSREF](#)
 22. Buliga-Finis ON, Ouatu A, Badescu MC, et al. Beyond the cardiorenal syndrome: pathophysiological approaches and biomarkers for renal and cardiac crosstalk. *Diagnostics (Basel)* 2022;12:773.
[PUBMED](#) | [CROSSREF](#)
 23. Martin L, Seton G, Aldred B, et al. When body mass index fails to measure up: perinephric and periumbilical fat as predictors of operative risk. *Am J Surg* 2016;212:1039-46.
[PUBMED](#) | [CROSSREF](#)
 24. Sun X, Han F, Miao W, Hou N, Cao Z, Zhang G. Sonographic evaluation of para- and perirenal fat thickness is an independent predictor of early kidney damage in obese patients. *Int Urol Nephrol* 2013;45:1589-95.
[PUBMED](#) | [CROSSREF](#)