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Original Article

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Perirenal Fat and Kidney Function Deterioration in Patients With Acute Decompensated Heart Failure

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Conflict of Interest
The authors have no financial conflicts of interest.

ABSTRACT

Background and Objectives: The thick perirenal fat pad can induce high intracapsular pressure and cause compression of the renal vasculature and resultant congestive nephropathy. The current study investigated the association of perirenal fat thickness with kidney dysfunction in patients with acute decompensated heart failure (ADHF).
Methods: Data from 266 patients hospitalized with ADHF were analyzed. Patients were divided into two groups according to the glomerular filtration rate (GFR) at admission (preserved kidney function [GFR ≥60 mL/min/1.73 m^2] and reduced kidney function [GFR <60 mL/min/1.73 m^2] groups). Right and left posterior perirenal fat thicknesses were measured using computed tomography, and their average values were calculated. Associated factors with reduced kidney function was assessed by logistic regression model, presenting with odds ratio (OR) and confidence interval (CI).
Results: Increasing age (OR, 1.08; 95% CI, 1.04–1.12; p<0.001), diabetes mellitus (OR, 2.46; 95% CI, 1.18–5.12; p<0.017), increased log N-terminal pro-B-type natriuretic peptide (NT-proBNP) (OR, 1.82; 95% CI, 1.32–2.52; p<0.001), and increased average perirenal fat thickness (OR, 1.11; 95% CI, 1.06–1.16; p<0.001) were independently associated with reduced kidney function. In the subgroup analyses, patients over 70 years old, the ratio of mitral-to-mitral annular velocity >15, elevated log NT-proBNP had a significantly higher association with increased perirenal fat thickness with reduced kidney function.
Conclusions: Thick perirenal fat pads were independently associated with kidney function deterioration in patients hospitalized with ADHF.

Keywords: Heart failure; Kidney; Adipose tissue

INTRODUCTION

The term cardiorenal syndrome describes a spectrum of disorders involving the heart and kidneys, in which acute or chronic dysfunction in the heart or kidneys may induce dysfunction in other organs.[1,2] Five phenotypes have been classified, and type 1 cardiorenal syndrome was defined as acute worsening of cardiac function leading to kidney dysfunction. In clinical practice, acute kidney injury frequently occurs in patients with

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acute decompensated heart failure (ADHF).[3] Kidney dysfunction in heart failure (HF) has traditionally been believed to result from decreased kidney perfusion and is related to hormonal and neural changes, and persistent renal venous congestion has been regarded as a more important hemodynamic contributor to the development of kidney dysfunction.[4-6]

Perirenal fat is a fat pad surrounding the kidneys in the retroperitoneal space and is located between the renal fibrous membrane and the renal fascia.[7] Recent epidemiological studies revealed that perirenal fat is a risk predictor of cardiovascular disease (CVD), independent of common clinical variables.[8] The thickness of perirenal fat surrounding the kidney and accumulated fat volume in the renal sinus have been associated with various chronic diseases, including chronic kidney disease (CKD), arteriosclerosis, hypertension, and the onset of diabetes mellitus.[8,9] It has recently suggested that perirenal fat tissue plays a role in acute kidney function deterioration in patients with ADHF by compressing the renal vasculature, leading to pathologic activation of the renin-angiotensin-aldosterone system and reduced renal perfusion,[7] even though its role in patients with ADHF needs further investigation.

It can be speculated that a thick perirenal fat pad might induce high intracapsular pressure more easily and cause compression of the renal vasculature and resultant congestive nephropathy. We therefore hypothesized that ADHF patients with a thick perirenal fat pad might be more vulnerable to kidney function deterioration than those with a thin pad. As perirenal fat thickness can be easily measured using computed tomographic images, the current study aimed to investigate the association between perirenal fat thickness assessed by computed tomography (CT) and kidney dysfunction in patients hospitalized with ADHF. In addition, we assessed the characteristics correlated with perirenal fat thickness in the population.

METHODS

Study population

We analyzed the data of patients hospitalized with ADHF between February 2019 and April 2022 at a single center for CVD in Korea. The exclusion criteria were as follows: acute myocardial infarction, aborted sudden cardiac death, hypertrophic cardiomyopathy, peripartum cardiomyopathy, active infective endocarditis, significant organic valvular heart disease, prosthetic heart valves, isolated right ventricular failure, single kidney, history of kidney transplantation, and known CKD. Among the 365 patients with ADHF without known CKD, 99 who lacked CT data covering fields at the kidney level within 6 months of index admission were also excluded. CKD was defined as glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 for 3 months or more prior to the index admission. Ultimately, 266 patients hospitalized with ADHF were included in the final analysis. Patients were divided into 2 groups according to the GFR at admission (preserved kidney function [GFR ≥60 mL/min/1.73 m^2] and reduced kidney function [GFR <60 mL/min/1.73 m^2] groups).

This study was approved by the ethics committee of our institution. The need for informed consent was waived because of 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. Medication history before index admission was obtained regarding angiotensin converting enzyme inhibitor (ACEI),

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angiotensin receptor antagonist (ARB), angiotensin receptor neprilysin inhibitor (ARNI), and diuretics. 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. HF was categorized according to left ventricular (LV) ejection fraction (EF) as follows: HF with preserved EF (HFpEF), LVEF ≥50%; HF with reduced EF (HFrEF), LVEF ≤40%; and HF with mildly reduced EF (HFmrEF), LVEF 41–49%.[10]

Laboratory tests, including hemoglobin, creatinine, aspartate transaminase, alanine transaminase, and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels, were obtained at admission. Kidney function was defined by the estimated GFR, calculated using the formula developed and validated in the Modification of Diet in Renal Disease study as follows[11]: GFR (mL/min/1.73 m^2)=186.3×(Serum Creatinine, mg/dL)$^{-1.154}$×Age$^{-0.203}$×(0.742, if female). NT-proBNP levels were logarithmically transformed to achieve a normal distribution.

Imaging modalities

Data from the first transthoracic echocardiography after the index admission were used in the analysis. The mean time interval between admission and echocardiography performance was 1.2±1.5 days. Two-dimensional and Doppler echocardiography were performed to assess cardiac structure and function according to the guidelines of the American Society of Echocardiography.[12] LV end-diastolic dimension (EDD) and LV end-systolic dimension (ESD) were measured from 2-dimensional images. LVEF 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.[12] The LV mass index was defined as the LV mass indexed to body surface area. Left atrial volume was calculated using the biplane area–length method. According to the guidelines, 2-dimensional volumetric measurements were based on left atrial area measurements using tracings of the blood-tissue interface and left atrial lengths on apical 4- and 2-chamber views.[12] Left atrial volume index (LAVI) was defined as the left atrial volume indexed to body surface area.

The mitral inflow velocities were obtained using pulse-wave Doppler in the apical four-chamber view. Mitral early diastolic (E) velocity and peak early diastolic mitral annular velocity (e′) were measured. We calculated the E/e′ ratio, which is a measure of LV filling pressure, by dividing E velocity by e′ velocity. The calculated systolic pulmonary artery pressure (SPAP) was defined as: 4×(maximum velocity of the tricuspid regurgitation [TR] jet)^2+right atrial pressure. Right atrial pressure was estimated by measuring the inferior vena cava diameter and he associated respiratory changes.[13]

The mean time interval between admission and CT performance was 0.9±0.1 months (median, 0 months; interquartile range, 0–6 months). CT images were used for perirenal fat thickness analysis. The mean time interval between admission and CT acquisition was 0.7±2.8 months. 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 (**Figure 1**).[14] The average perirenal fat was calculated using the right and left posterior perirenal fat thicknesses.

Statistics

Demographic characteristics were reported as percentages or means±standard deviations. The patient groups were compared using χ^2 statistics for categorical variables and Student's *t*-test for continuous variables. To determine potential independent associations between the variables and reduced kidney function, binary logistic regression was applied. Variables

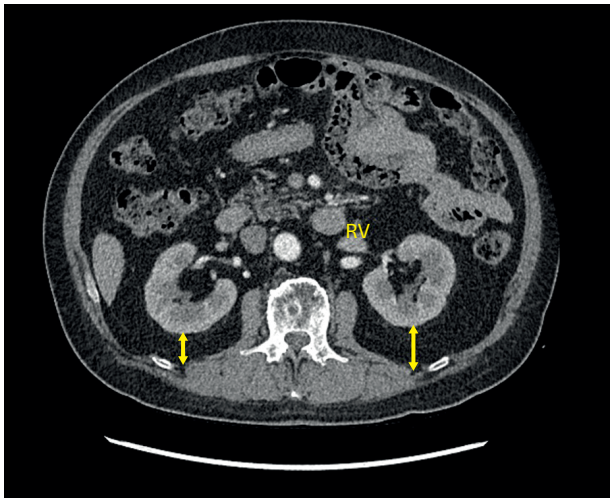

Figure 1. Method of measuring posterior perirenal fat thickness. Yellow double-headed arrows indicate the posterior perirenal fat thickness.
RV = renal vein.

with p values <0.1 in the univariable analysis were entered into the multivariable binary logistic regression model, and the odds ratios (ORs) and 95% confidence intervals (CIs) were reported. The interaction between the average perirenal fat thickness and the adjusting factors was evaluated. To determine potential independent correlation between the variables and perirenal fat thickness, linear logistic regression was applied. Variables displaying a p value <0.2 in univariable analysis were entered into the multivariable linear logistic regression model. We fitted a cubic spline model for assessment of correlation between glomerular filtration rate and the mean renal fat thickness. To evaluate intra- and interobserver reproducibility for renal fat thickness measurement, the intraclass correlation coefficient (ICC) was calculated. Good correlation was defined as an ICC >0.8. Statistical significance was set at p<0.05.

RESULTS

Patient characteristics

Among the 266 patients hospitalized with ADHF, 198 (87.6%) were initially diagnosed with HF and 28 (12.4%) with acute decompensation of previously diagnosed HF. The mean patient age was 77±12 years, and 135 patients (59.2%) were women. There were 120 patients with preserved kidney function and 106 with reduced kidney function. Mean GFR was 82.1±14.5 mL/min/1.73 m^2 and 41.6±10.7 mL/min/1.73 m^2 in the preserved and reduced kidney function groups, respectively.

Table 1 summarizes the baseline characteristics of the study population. There were no significant differences in the prevalence of sex, hypertension, diabetes mellitus, atrial fibrillation, BMI, systolic and diastolic BP, medications at admission, etiology of HF, and type of HF between the preserved and reduced kidney function groups (all p>0.05). Patients with reduced kidney function were older than those with preserved kidney function (81±8 vs. 73±14 years, p<0.001). Echocardiographic variables, including LVEDD, LVESD, LVEF, LV mass index, LAVI, E/e′, peak TR velocity, and SPAP, were comparable between the groups. Log NT-proBNP (8.9±1.4 pg/mL vs. 8.4 pg/mL, p<0.001) and average perirenal fat thickness (13.4 mm

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Table 1. Baseline characteristics

Variables	Overall	Kidney function at admission		
		Preserved (GFR ≥60 mL/min/1.73 m²)	Reduced (GFR <60 mL/min/1.73 m²)	p value
No. of patients	226	120	106	
Demographics				
Age (years)	77±12	73±14	81±8	<0.001*
Female sex	135 (59.2)	68 (56.7)	67 (63.2)	0.317
Hypertension	88 (38.9)	46 (38.3)	42 (39.6)	0.843
Diabetes mellitus	59 (26.1)	25 (20.8)	34 (32.1)	0.055
Atrial fibrillation	96 (42.5)	51 (42.5)	45 (42.5)	0.994
BMI (kg/m²)	23.6±5.4	23.5±6.2	23.6±4.5	0.997
Systolic BP (mm Hg)	131.8±21.2	130.6±21.5	133.2±20.7	0.350
Diastolic BP (mm Hg)	76.1±14.4	77.7±15.5	74.3±12.9	0.072
HF category				0.097
HFrEF	119 (52.7)	67 (55.8)	52 (49.1)	
HFmrEF	37 (16.4)	23 (19.2)	14 (13.2)	
HFpEF	70 (31.0)	30 (25.0)	40 (37.7)	
Etiology				0.876
Ischemic	54 (23.9)	28 (23.3)	26 (24.5)	
Non-ischemic	172 (76.1)	92 (76.7)	80 (75.5)	
NYHA functional class				0.117
III	37 (16.4)	24 (20.0)	13 (12.3)	
IV	189 (83.6)	96 (80.0)	93 (87.7)	
Medication				
ACEI	5 (2.2)	3 (2.5)	2 (1.9)	0.753
ARB	68 (30.1)	30 (25.0)	38 (55.9)	0.076
ARNI	2 (0.1)	2 (1.7)	0 (0)	0.110
Beta blocker	59 (26.1)	29 (24.2)	30 (28.2)	0.480
Diuretics	53 (3.5)	22 (18.3)	31 (29.2)	0.053
Echocardiography				
LVEDD (mm)	54.3±8.5	54.9±8.6	53.6±8.4	0.255
LVESD (mm)	42.2±11.8	43.4±11.7	40.8±11.7	0.095
LVEF (%)	39.6±17.4	37.6±16.9	41.9±17.9	0.068
LV mass index (g/m²)	129.7±40.5	127.6±37.3	132.0±43.9	0.416
LAVI (mL/m²)	58.3±20.5	58.5±22.2	58.2±18.4	0.919
E/e′	20.7±9.2	20.3±9.1	21.2±9.3	0.464
Peak TR velocity (m/s)	2.7±0.5	2.7±0.5	2.8±0.5	0.226
SPAP (mm Hg)	38.0±13.3	37.0±13.6	39.2±13.0	0.224
Laboratory findings				
GFR (mL/min/1.73 m²)	63.1±24.0	82.1±14.5	41.6±10.7	<0.001*
Log NT-proBNP (pg/mL)	8.6±1.2	8.4±1.1	8.9±1.4	<0.001*
Hemoglobin (g/dL)	12.0±2.2	12.5±2.1	11.5±2.0	<0.001*
Aspartate transaminase (IU/L)	49.0±62.4	43.6±33.5	55.1±83.7	0.168
Alanine transaminase (IU/L)	36.2±69.6	30.9±35.4	42.3±94.2	0.219
CT				
Right perirenal fat thickness (mm)	10.2±7.9	8.1±6.6	12.5±8.7	<0.001*
Left perirenal fat thickness (mm)	11.7±8.7	9.3±7.5	14.4±9.2	<0.001*
Average perirenal fat thickness (mm)	10.9±8.1	8.7±6.9	13.4±8.7	<0.001*

Values are presented as number with percentages or means±standard deviations.
GFR = glomerular filtration rate; BMI =body mass index; BP = blood pressure; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; NYHA = New York Heart Association; ACEI = Angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; LVEDD = left ventricular end-diastolic dimension; LVESD = left ventricular end-systolic dimension; LVEF = left ventricular ejection fraction; LV = left ventricular; LAVI = left atrial volume index; E/e′ = the ratio of early diastolic mitral inflow to mitral annular velocity; TR = tricuspid regurgitation; SPAP = systolic pulmonary artery pressure; NT-proBNP = N-terminal pro-B-type natriuretic peptide; CT = computed tomography.
*p value <0.05.

vs. 8.7 mm, p<0.001) were all higher and hemoglobin was lower (11.5±2.0 g/dL vs. 12.5±2.1 g/dL, p<0.001) in patients with reduced kidney function compared to those with preserved kidney function.

Factors associated with reduced kidney function

Table 2 shows the results of the univariable and multivariable logistic regression analyses for factors associated with reduced kidney function in patients hospitalized with ADHF. In multivariate analysis, increasing age (OR, 1.08; 95% CI, 1.04–1.12; p<0.001), diabetes mellitus (OR, 2.46; 95% CI, 1.18–5.12; p<0.017), increased log NT-proBNP (OR, 1.82; 95% CI, 1.32–2.52; p<0.001), and increased average perirenal fat thickness (OR, 1.11; 95% CI, 1.06–1.16; p<0.001) were associated with reduced kidney function, even after adjusting for diastolic BP, HF category, LVESD, and LVEF.

Correlation between GFR and the mean perirenal fat thickness are shown in **Figure 2**. Cubic spline analysis showed a negative linear correlation between the mean perirenal fat thickness and the GFR. The GFR demonstrated statistically significant association according to the quartiles of the mean perirenal fat thickness (p for trend<0.001).

Figure 3 illustrates the subgroup analysis of the association between perirenal fat and reduced kidney function. There were no statistically significant differences when the groups were stratified according to sex, hypertension, diabetes mellitus, or HF categories (all p for interaction>0.05). In the subgroup analyses based on age, patients over 70 years old (OR, 1.11; 95% CI, 1.06–1.17; p<0.001) had a significantly higher association with increased perirenal fat thickness with reduced kidney function compared to younger patients (OR, 1.07; 95% CI, 0.86–1.34; p=0.526) (p for interaction=0.025). Patients with E/e′ >15 (OR, 1.15; 95% CI, 1.09–1.22; p<0.001) demonstrated a significantly higher association with increased perirenal fat thickness and reduced kidney function compared to those with lower E/e′ (OR, 0.91; 95% CI, 0.79–1.06; p=0.347) (p for interaction=0.019). In the subgroup analyses based on log NT-proBNP (median value, 8.6 pg/mL), patients with log NT-proBNP above median

Table 2. Factors associated with reduced kidney function in patients with acute decompensated HF

Variable	Univariable			Multivariable		
	OR	95% CI	p value	OR	95% CI	p value
Age, per year	1.07	1.04–1.10	<0.001*	1.08	1.04–1.12	<0.001*
Female sex	0.76	0.45–1.30	0.317	-	-	-
Hypertension	1.06	0.62–1.80	0.843	-	-	-
Diabetes mellitus	1.79	0.98–3.27	0.056	2.46	1.18–5.12	0.017*
Atrial fibrillation	1.00	0.95–1.05	0.977	-	-	-
BMI	1.00	0.95–1.05	0.997	-	-	-
Systolic BP	1.01	0.99–1.02	0.349	-	-	-
Diastolic BP	0.98	0.97–1.00	0.075	0.99	0.96–1.01	0.987
HFrEF (vs. HFpEF)	1.72	0.95–3.12	0.075	1.61	0.29–8.95	0.586
Ischemic etiology	1.07	0.58–1.97	0.834	-	-	-
NYHA functional class IV	1.79	0.86–3.72	0.120	-	-	-
LVEDD, per 1 mm increase	0.98	0.95–1.01	0.982	-	-	-
LVESD, per 1 mm increase	0.98	0.96–1.00	0.097	1.06	1.00–1.12	0.051
LVEF, per 1% increase	1.01	1.00–1.03	0.069	1.05	0.99–1.11	0.142
LV mass index, per 1 g/m^2 increase	1.00	1.00–1.01	0.341	-	-	-
LAVI, 1 mL/m^2 increase	1.00	0.99–1.01	0.919	-	-	-
E/e′, per 1 unit increase	1.00	0.98–1.04	0.463	-	-	-
Hemoglobin, per 1 g/dL increase	0.90	0.79–1.01	0.182	-	-	-
SPAP, per 1 mmHg increase	1.01	0.99–1.03	0.223	-	-	-
Log NT-proBNP, per 1 pg/mL increase	1.44	1.14–1.81	0.003*	1.82	1.32–2.52	<0.001*
Average perirenal fat thickness, per 1 mm increase	1.02	1.04–1.13	<0.001*	1.11	1.06–1.16	<0.001*

HF = heart failure; OR = odds ratio; CI = confidence interval; BMI = body mass index; BP = blood pressure; HFrEF = heart failure with reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; NYHA = New York Heart Association; LVEDD = left ventricular end-diastolic dimension; LVESD = left ventricular end-systolic dimension; LVEF = left ventricular ejection fraction; LV = left ventricular; LAVI = left atrial volume index; E/e′ = the ratio of early diastolic mitral inflow to mitral annular velocity; TR = tricuspid regurgitation; SPAP = systolic pulmonary artery pressure; NT-proBNP = N-terminal pro-B-type natriuretic peptide.
*p value <0.05.

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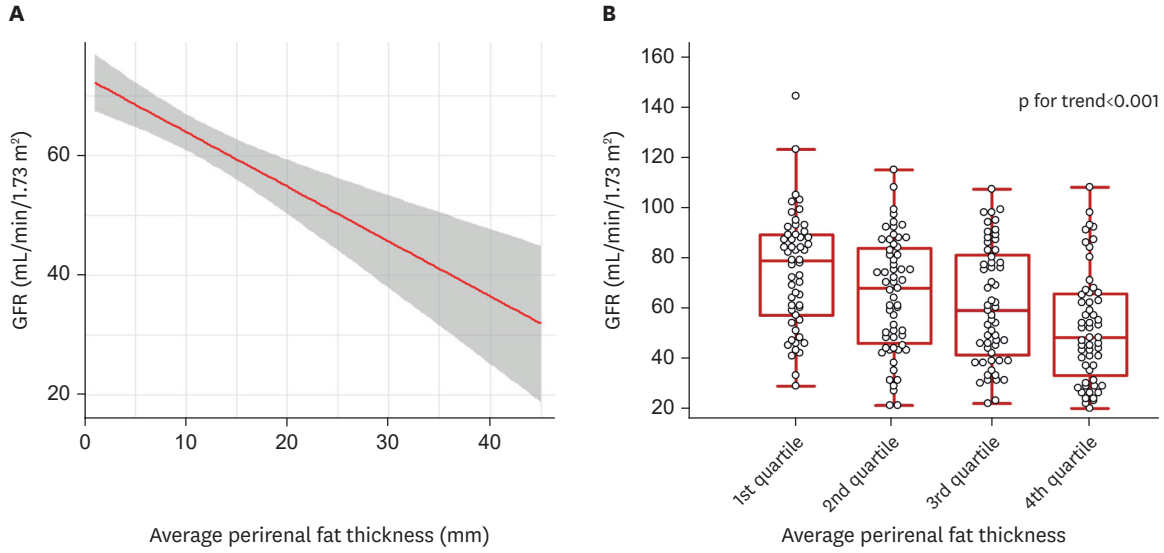

Figure 2. Correlation between glomerular filtration rate and average perirenal fat thickness.
(A) Cubic spline regression analysis. (B) Changes in glomerular filtration rate according to quartile of average perirenal fat thickness. Shadow area is the 95% confidence interval of the predicted GFR (solid red line). Vertical bars represent 5th to 95th percentiles, boxes represent interquartile range, and horizontal lines represent the median.
GFR = glomerular filtration rate.

(OR, 1.20; 95% CI, 1.10–1.31; p<0.001) demonstrated a significantly higher association with increased perirenal fat thickness and reduced kidney function compared to those with log NT-proBNP below median (p for interaction<0.001).

To reconfirm our data, we performed additional analysis with different cutoff values of GFR of 35 mL/min/1.32 m² (**Supplementary Tables 1** and **2**), which showed similar results performed with the cutoff value of GFR 60 mL/min/1.32 m².

Factors correlated with perirenal fat thickness

The clinical characteristics correlated with the average perirenal fat thickness are presented in **Table 3**. In the univariate analysis, BMI, systolic BP, and HFpEF were positively correlated with perirenal fat thickness. However, the only factor showing an independent correlation with increasing perirenal fat thickness was BMI, even after adjusting for sex, coronary artery disease, systolic BP, and HF categories in the multivariable analysis (p<0.001).

Table 3. Characteristics correlated with perirenal fat thickness

Variable	Univariable			Multivariable		
	Beta	t	p value	Beta	t	p value
Age	0.052	0.775	0.439	-	-	-
Female sex	−0.092	−1.380	0.169	−0.093	−1.456	0.147
Hypertension	0.034	0.508	0.612	-	-	-
Diabetes mellitus	0.058	0.868	0.386	-	-	-
Atrial fibrillation	−0.025	−0.371	0.711	-	-	-
BMI	0.297	4.647	<0.001*	0.269	3.973	<0.001*
Systolic BP	0.142	2.146	0.033*	0.049	0.735	0.463
Diastolic BP	0.045	0.680	0.497	-	-	-
HFpEF	0.137	2.067	0.040*	0.108	1.685	0.093
Ischemic etiology	0.086	1.294	0.197	0.096	1.504	0.134

BMI = body mass index; BP = blood pressure; HFpEF = heart failure with preserved ejection fraction.
*p value <0.05.

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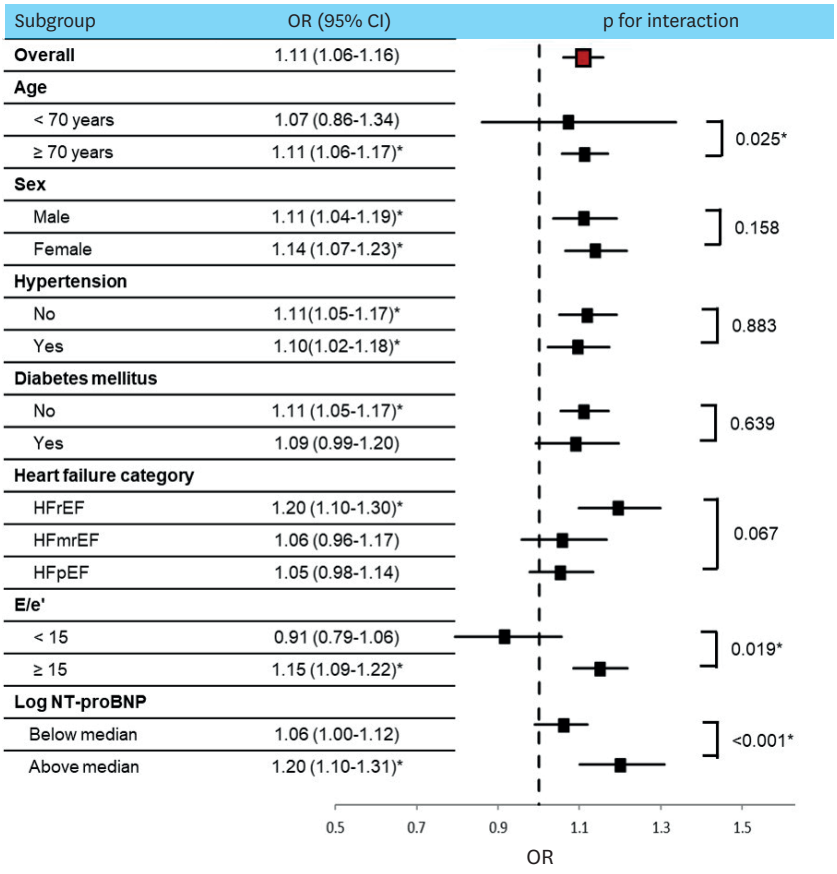

Figure 3. Subgroup analysis for association of average perirenal fat thickness with reduced kidney function.
OR = odds ratio; CI = confidence interval; E/e′ = the ratio of early diastolic mitral inflow to mitral annular velocity; NT-proBNP = N-terminal pro-B-type natriuretic peptide.

Reproducibility of renal fat measurement

The ICCs for intra-observer and interobserver reproducibility of renal fat measurement were 0.998 (95% CI, 0.993–1.000) and 0.994 (95% CI, 0.977–0.999), respectively (all p<0.001).

DISCUSSION

The principal findings of the current study are that 1) a thick posterior perirenal fat pad was independently associated with kidney function deterioration in patients hospitalized with ADHF; 2) the association was more prominent in the subgroups of patients over 70 years and those with evidences of congestion reflected by high E/e′ and NT-proBNP; and 3) the BMI was the only factor correlated with perirenal fat thickness in those populations.

The heart and kidneys are closely related and interdependent; the term cardiorenal syndrome describes this phenomenon.[15] Type 1 acute cardiorenal syndrome is characterized by acute worsening of cardiac function, leading to renal dysfunction.[1] Traditionally, the pathophysiology of kidney dysfunction in HF is believed to result from decreased renal perfusion and associated hormonal and neural changes.[16] However, recently, persistent venous congestion has been identified as a main contributor to cardiorenal syndrome[4,5] and animal models support that congestion is a more important determinant of kidney

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dysfunction than renal perfusion.[17] Elevated central venous pressure has been reported to result in renal venous hypertension, increased renal resistance, and ultimately impaired intrarenal blood flow in patients with ADHF.[4,18] Boorsma et al.[7] recently suggested the renal tamponade hypothesis and renal decapsulation therapy, which have demonstrated benefits in animals,[19] making it an interesting, novel treatment for HF, that requires further investigation.

Although congestive nephropathy is a potentially reversible form of renal dysfunction due to effective decongestion, its diagnosis is challenging. There is no gold standard for assessing renal venous congestion.[6] The invasive assessment using a wireless implantable hemodynamic monitoring system has been suggested, but limited availability, high cost, and invasive nature of the procedure limit its application.[20]

Perirenal fat is a fat pad surrounding the kidneys in the retroperitoneal space, located between the renal fibrous membrane and the renal fascia.[7] Perirenal fat shares the same developmental origin as typical visceral fat, but differs regarding histology, physiology, and functions.[8] Perirenal fat is separated from the peritoneum by the renal fascia, whereas visceral fat is typically located in the intraperitoneal space.[21]

The kidneys are low-resistance circuits that are known to receive a disproportionately large fraction of cardiac output.[1] It has been suggested that elevated intra-abdominal pressure in the presence of ADHF may contribute to renal dysfunction by causing renal compression and reduced perfusion[22] and the rigidity of the renal capsule plays a central role in congestion-induced kidney damage.[7] Our study suggests that a thick perirenal fat pad might load more burden to the kidney in the setting of ADHF by occupying a large intracapsular space. That is, the thick perirenal fat pad can accelerate the increase in renal pressure by prohibiting the expansion of the kidney within the renal capsule and causing pressure to be reflected inward.

We found that increasing perirenal fat thickness was associated with deterioration of kidney function in hospitalized patients with ADHF, and this relationship was more pronounced in the population with high E/e′ and NT-proBNP. The E/e′ ratio on echocardiography and NT-proBNP can be used to diagnose congestive states in patients with HF.[23] E/e′ directly correlates with pulmonary capillary wedge pressure, with an E/e′ >15 correlating with a pulmonary capillary wedge pressure of ≥15 mmHg.[24,25] Interestingly, we found that the association between perirenal fat thickness and reduced kidney function was significant in patients with evidence of high E/e′ (>15) and elevated NT-proBNP above median, while this association was blunted in the population with lower E/e′ ratio and NT-proBNP. This fact might further support our hypothesis that a thick perirenal fat pad induces high intracapsular pressure more easily, facilitating compression of the renal vasculature and resultant congestive nephropathy.

CT is a valuable imaging tool for the diagnosis of acutely ill patients who present with symptoms of chest pain or dyspnea, which are common symptoms of ADHF. Therefore, many patients hospitalized with ADHF frequently undergo CT for various purposes. Posterior perirenal fat thickness can be easily measured using previously acquired CT images without an additional reconstruction process. We found that the measurement of perirenal fat thickness could be a novel surrogate marker for the detection of vulnerable patients with ADHF who are prone to kidney function deterioration. Considering the fact that biomarkers for the differential diagnosis of acute kidney injury in ADHF are scarce, the simple

measurement of perirenal fat thickness could provide additional understanding regarding diagnosis, treatment strategies, and prognostic value for renal injury in patients with ADHF. Furthermore, perirenal fat thickness can be measured using other modalities, such as ultrasound[26] or magnetic resonance imaging[14] further studies are required regarding the role of perirenal fat assessed by various imaging modalities in patients with ADHF.

Obesity is a known risk factor for HF and contributes to the onset of cardiorenal syndrome.[27] Visceral adiposity is associated with a greater risk of cardiorenal morbidity than subcutaneous adiposity.[28] Perirenal fat has been reported as an indirect measurement that correlates with visceral fat[29,30] although perirenal fat and visceral fat differ in various aspects.[6] Therefore, the differential role of perirenal fat and intra-abdominal fat in renal function deterioration in HF requires further investigation. Increasing BMI was independently associated with increasing perirenal fat thickness in the current study, and it would be worthwhile to investigate whether weight reduction in patients with high perirenal fat thickness could decrease the perirenal fat pad, resulting in renal decapsulation effect, and finally reducing cardiorenal syndrome in patients with various categories of HF.

The main limitation of the current study is that the results were based on retrospective data analysis. However, the patients' medical records, echocardiography, and CT findings were carefully reviewed to minimize biases. Second, echocardiography was not performed on the same day in all patients. Hemodynamic variables, especially E/e′, might be influenced by HF treatment, although persistent elevation of E/e′ after a prolonged time interval might be evidence of more advanced congestion. Furthermore, the interval between the GFR measurement and echocardiography performance was not prolonged, as reflected by the mean time interval of approximately one day in our study. Third, CT was performed by each clinician's decision and the reason for CT was not clearly identified in many cases, due to the retrospective nature of this study. Fourth, the perirenal fat thickness was measured at a single plane in the posterior direction, while the perirenal fat was located around the kidney. Studies using multidirectional or volumetric measurements are warranted for more accurate measurement of the perirenal fat pad. However, perirenal fat thickness measured using CT at the level of the renal veins has been reported as a simple and reliable estimate of perirenal fat volume,[31] and therefore, our simple measurement method would be clinically useful and easy to apply. Finally, the number of the study population was not enough to calculate the discrimination power. Further studies are warranted with an enough sample size study population in the future.

In conclusion, a thick perirenal fat pad was independently associated with deterioration of kidney function in patients hospitalized with ADHF and the association was more prominent in subgroups of patients over 70 years and those with the evidence of congestion. The measurement of posterior perirenal fat thickness may be a novel surrogate marker for identifying patients with ADHF who are prone to kidney function deterioration.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Baseline characteristics

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Supplementary Table 2

Factors associated with reduced kidney function of GFR <35 mL/min/1.73 m^2 in patients with acute decompensated HF

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