

# Analysis of the clinical features and risk factors of kidney injury in patients with chronic heart failure—a retrospective cohort study

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**Background:** Heart failure (HF) often leads to kidney injury and increased morbidity and mortality. Factors contributing to kidney injury in HF patients had not been elucidated completely. This study sought to comprehensively evaluate the risk factors and clinical features of kidney injury in patients with chronic heart failure (CHF) and to provide more evidence for the management of these patients.

**Methods:** Adult patients with CHF admitted to Beijing Anzhen Hospital, Capital Medical University from January 2022 to May 2022 were included in this study. The primary endpoints were the independent risk factors for the development of kidney injury. A multivariate logistic regression model was used for the exploration of the risk factors.

**Results:** A total of 193 patients were included in this study, of whom 86 (44.5%) developed kidney injury. The independent risk factors for kidney injury in patients with CHF included sex (male) [odds ratio (OR): 4.30, 95% confidence interval (CI): 1.72–10.7, P=0.001], hypertension (OR: 3.68, 95% CI: 1.64–8.29, P=0.001), and stroke (OR: 3.82, 95% CI: 1.25–11.6, P=0.01). Kidney injury was significantly positively correlated with age (OR: 1.03, 95% CI: 1.008–1.06, P=0.01) and potassium (OR: 3.70, 95% CI: 1.58–8.67, P=0.002), and significantly negatively correlated with angiotensin receptor blocker (ARB) application (OR: 0.26, 95% CI: 0.11–0.61, P=0.001), serum albumin concentration (OR: 0.88, 95% CI: 0.81–0.96, P=0.005), hemoglobin concentration (OR: 0.97, 95% CI: 0.95–0.99, P=0.006), and left ventricular ejection fraction (LVEF; OR: 0.95, 95% CI: 0.92–0.98, P=0.01).

**Conclusions:** Kidney injury occurred in more than half of the patients with CHF during hospitalization. The independent risk factors for kidney injury in the CHF patients included sex (male), hypertension, and stroke. Kidney injury was positively correlated with age and serum potassium, and negatively correlated with serum albumin, hemoglobin concentration, LVEF, and ARB application.

Keywords: Chronic heart failure (CHF); kidney injury; risk factors

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#### Introduction

Heart failure (HF) is a leading cause of morbidity and mortality worldwide, and has a 5-year case fatality rate approaching 50% (1). A recent worldwide survey reported that the median prevalence of HF was 17.20 (interquartile range, 14.30–21) cases per 1,000 people (2), and that approximately 40 million people are affected by HF worldwide (3). During the development of HF, fluid overload

causes damage to the heart and kidneys (4), which leads to further deteriorations in the functions of both organs and increases the morbidity and mortality of patients (5). Approximately 50% of patients with chronic heart failure (CHF) with reduced or preserved left ventricular ejection fraction (LVEF) have a glomerular filtration rate (GFR) of <60 mL/min/1.73 m<sup>2</sup> (6). Acute kidney injury (AKI) occurs in approximately 43–57% of hospitalized patients with acute decompensated CHF (7). If not treated in time, the concomitant kidney injury can significantly increase the short- and long-term mortality of patients with CHF (8). Thus, timely evaluation of renal function in patients with CHF is essential in the evaluation of the condition and in the determination of treatment measures.

Serum creatinine (sCr) is one of the most commonly used indicators of renal function. A published study has shown that an increase >20% in sCr (compared to the baseline) in patients with CHF is strongly associated with a significant increase in mortality (9).

Thus, a better understanding of the role of cardio-kidney interactions in the development, disease progression, and prognosis of HF symptoms is critical. Correct clinical decision making relies on early risk assessment and diagnosis (10). Thus, it is clinically important to properly assess the risk factors for kidney injury in patients with CHF in an appropriate clinical context (11). Previous studies have shown that vascular disease, thiazide diuretic use, baseline blood urea nitrogen >9 mmol/L (12), elevated sCr on admission, a poor New York Heart Association (NYHA)

#### Highlight box

#### Key findings

 The independent risk factors for kidney injury in patients with CHF included sex (male), hypertension, stroke, an advanced age, elevated serum potassium concentration, decreased serum albumin concentration, hemoglobin concentration, and LVEF.

#### What is known and what is new?

- Patients with chronic heart failure are at increased risk for kidney injury.
- Our study identified novel independent risk factors for kidney injury in patients with chronic heart failure.

#### What is the implication, and what should change now?

 Renal injury can significantly affect the prognosis of patients with CHF. Thus, it is of great clinical significance to accurately identify high-risk groups early to enable appropriate preventive and therapeutic measures to be implemented. classification of cardiac function (13), a medical history of chronic kidney disease (CKD), spironolactone exposure, and higher doses of loop diuretics (14) are independent risk factors for kidney injury in patients with CHF. However, previous studies had been limited by small sample sizes and incomprehensive risk factors, leading to unclear elucidation of the correlation between chronic heart failure and kidney injury. It had been demonstrated that timely intervention for heart failure patients with kidney damage can reduce mortality and improve prognosis (15).

The present study sought to comprehensively evaluate the risk factors and clinical features of kidney injury in patients with CHF to provide a basis for disease evaluation and clinical decision making in such patients. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/ view/10.21037/jtd-23-1016/rc).

#### **Methods**

#### Study design

A retrospective cohort study was conducted. This study complied with the provisions of the Declaration of Helsinki (as revised in 2013) (16), and was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (No. KS2023001). All the patients signed the informed consent form.

#### Research subjects

Adult patients with CHF admitted to Beijing Anzhen Hospital, Capital Medical University from January 2022 to May 2022 were included as the study subjects.

## **Inclusion criteria**

To be eligible for inclusion in this study, the patients had to meet the following inclusion criteria: (I) have been diagnosed with CHF, including (i) HF with a reduced ejection fraction (EF) <40%, (ii) HF with a median EF of 40–49%), and (iii) HF with a preserved EF  $\geq$ 50%); (II)  $\geq$ 18 years; and (III) have signed the informed consent form.

#### **Exclusion criteria**

Patients were excluded from the study if they met any of the following exclusion criteria: (I) had undergone a heart transplantation; (II) had a tumor; (III) had a serious infectious disease; (IV) had a history of chronic kidney

## 3936

disease (CKD) [defined as: unexplained decrease in GFR (<60 mL/min/1.73 m<sup>2</sup>) for more than 3 months]; (V) had a liver disease; and/or (VI) with missing data such as demographics and clinical endpoints

#### Diagnostic criteria and definitions

#### Evaluation and diagnosis of CHF

The evaluation and diagnosis of CHF was based on each patient's history, physical examination, laboratory tests, cardiac imaging, and functional tests. The specific diagnostic process is described in the *Chinese Guidelines for the Diagnosis and Treatment of Heart Failure 2018* (17).

#### Methods for evaluating renal function

Renal function was evaluated based on the GFR using the following two types of assay measurements:

- (I) The estimation method: the following formulas of the CKD Epidemiology Collaboration (18) were used to calculate the eGFR:
  - Male eGFR = (140 age) × body weight (kg) ×1.23/sCr (µmoI/L)
  - (ii) Female eGFR = (140 age) × body weight (kg) ×1.03/sCr (µmoI/L)
- (II) The nuclear medicine measurement method: this method used renal dynamic imaging plus the GFR measurement.

## Definition and measurement of kidney injury

Kidney injury was defined as a GFR that decreased by  $\geq 25\%$  compared to the baseline (19). The eGFRs or measurements were performed daily during hospitalization and compared to the baseline levels.

#### Study endpoints

The primary endpoints of the study were the independent risk factors for the development of renal dysfunction (which was defined as a decreased GFR  $\geq 25\%$ ). The secondary endpoints were the primary clinical features of the CHF patients with kidney injury including comorbidities, vital signs, laboratory tests results, and severity of heart failure.

## Data collection

The variables that were collected for analyses were determined based on the clinical relevance and previous reports (12-14,20). The demographic characteristics, clinical

data, experimental examination results, echocardiography parameters, and medication information of the study subjects were collected from the electronic medical record system.

#### Statistical analysis

The continuous variables that conformed to the normal distribution are expressed as the mean  $\pm$  standard deviation, and are otherwise expressed as the median (interquartile range). The comparisons between the two groups were performed using the independent sample *t*-test or the non-parametric Mann-Whitney *U*-rank sum test. The categorical variables are presented as the numeric value and percentage, and the comparisons between the groups were performed using the chi-square test or Fisher's exact probability test.

Kidney injury (i.e., a GFR decrease  $\geq 25\%$ ) during hospitalization was used as the dependent variable, and each patient was assigned a value as follows: did not occur [0]/ occurred [1]. First, a univariate analysis was performed, and the independent variables with P values <0.1 were then included in the logistics regression model for the multivariate analysis. A multicollinearity analysis (21) was performed before the variables were included in the regression model, and the variables with a variance inflation factor >10 were excluded. Next, the variables were screened using the stepwise selection method, and the variables included in the model were independent influencing factors. Blood pressure, heart rate, N-terminal pro-B-type natriuretic peptide (NT-proBNP), diuretic use, diabetes, and other potential confounding factors were included in the model for adjustment. The overall goodness-of-fit of the model was evaluated by the Hosmer-Lemeshow test (22). A bilateral P value <0.05 was considered statistically significant. All the statistical analyses were performed using MedCalc® Statistical Software version 19.6.4 (MedCalc Software Ltd., Ostend, Belgium; https://www.medcalc.org; 2021).

#### **Results**

#### Inclusion of the baseline characteristics of the patients

A total of 254 patients with CHF were admitted during the study period, of whom 61 patients were excluded, and 193 met the inclusion criteria (*Figure 1*). The median age of the included patients was 65 [53–73] years, and 115 (59.6%) were men. The patients had a median systolic blood

#### Journal of Thoracic Disease, Vol 15, No 7 July 2023

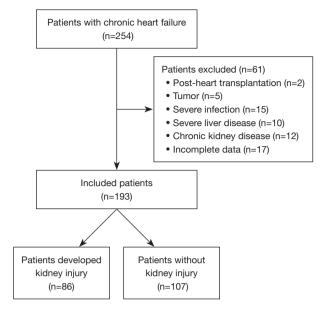


Figure 1 Flowchart of patient screening process.

pressure of 118 [105–130] mmHg, a median heart rate of 76 [65–86] beats per minute, and a median LVEF of 40% (40–60%). In total, 119 (61.7%) patients had NYHA Class III or above for cardiac function. The patients had a median baseline sCr of 88 [73–120] µmol/L and a median eGFR of 66 [36–92] mL/min/1.73 m<sup>2</sup>. There were 63 (32.6%), 101 (52.3%), 39 (20.2%), and 35 (18.1%) patients with underlying diabetes mellitus, hypertension, coronary heart disease, and stroke, respectively. The baseline characteristics of the patients are shown in *Table 1*.

### Univariate analysis results

Eighty-six (44.6%) patients developed kidney injury during the hospital stay. There were no statistically significant differences between the two groups in terms of the gender ratio, systolic blood pressure, total bilirubin, platelet count, and diuretic use. The prevalence of underlying diseases, age {69 [59–76] vs. 59 [49–69] years, P<0.01}, heart rate {79 [65–94] vs. 72 [66–81] beats/ minute, P=0.02}, NT-proBNP {4,799 [1,661–7,871] vs. 708 [284–2,239] pg/mL, P<0.01}, sCr {125 [110–169] vs. 76 [66–82] µmol/L, P<0.01}, serum potassium [4.3 (4.0– 4.6) vs. 4.0 (3.8–4.2) mmol/L, P<0.01], white blood cell count [7.45 (5.76–8.49)×10<sup>9</sup>/L vs. 6.6.11 (5.4–7.88)×10<sup>9</sup>/ L, P<0.01], and the neutrophil/lymphocyte ratio [3.7 (2.68–5.3) vs. 2.54 (2.05–3.8), P<0.01] were significantly higher in the kidney injury group than the control group. NYHA heart function classification {3 [2-3] vs. 3 [2-3], P<0.01}, albumin concentration [36.9 (34.4–39.5) vs. 41 (36.3–44) g/L, P<0.01], the eGFR {33 [20-47] vs. 89 [74–101] mL/min/1.73 m<sup>2</sup>, P<0.01}, hemoglobin concentration {122 [102-139] vs. 135 [122-152] g/L, P<0.01}, LVEF [40% (40–44%) vs. 40% (40–60%), P=0.01], and angiotensin receptor blocker (ARB) use [23.2% vs. 55.1%, P<0.01] were significantly lower in the kidney injury group than in the control group.

#### Multivariate logistic regression analysis results

The multivariate analysis demonstrated that the independent risk factors for kidney injury in patients with CHF included sex (male) (OR: 4.30, 95% CI: 1.72–10.7, P=0.001), hypertension (OR: 3.68, 95% CI: 1.64–8.29, P=0.001), and stroke (OR: 3.82, 95% CI: 1.25–11.6, P=0.01). Kidney injury was significantly positively correlated with age (OR: 1.03, 95% CI: 1.008–1.06, P=0.01), and potassium (OR: 3.70, 95% CI: 1.58–8.67, P=0.002), which was positively correlated with ARB application (OR: 0.26, 95% CI: 0.11–0.61, P=0.001). Additionally, kidney injury was negatively correlated with serum albumin concentration (OR: 0.88, 95% CI: 0.81–0.96, P=0.005), hemoglobin concentration (OR: 0.97, 95% CI: 0.92–0.98, P=0.01) (*Table 2*).

To reduce the confounding bias, the factors that might affect cardiac and renal function (i.e., blood pressure, heart rate, diabetes, NT-proBNP, and diuretic use) were introduced into a model that was adjusted for sex (male) (OR: 5.49, 95% CI: 2.02–14.9, P=0.0008), age (OR: 1.03, 95% CI: 1.005–1.07, P=0.02), hypertension (OR: 4.42, 95% CI: 1.71–11.43, P=0.002), stroke (OR: 6.67, 95% CI: 1.80–24.6, P=0.004), ARB application (OR: 0.28, 95% CI: 0.11–0.71, P=0.007), albumin (OR: 0.89, 95% CI: 0.81–0.98, P=0.01), hemoglobin (OR: 0.97, 95 % CI: 0.95–0.99, P=0.008), and potassium (OR: 4.53, 95% CI: 1.76–11.6, P=0.001). The statistical significance of LVEF (OR: 0.96, 95% CI: 0.92–1.004, P=0.08) was not affected (*Table 3*).

#### Discussion

In this prospective observational cohort study, 193 patients with CHF were included, of whom, 86 (44.6%) developed kidney injury during the hospital stay. The multivariate logistic regression analysis results demonstrated that the independent risk factors for kidney injury in patients with 3938

Characteristic indicators	Overall (N=193)	Kidney injury group (n=86)	Control group (n=107)	P value
Male	115 (59.6)	55 (63.9)	60 (56.1)	0.26
Age (years)	65 [53–73]	69 [59–76]	59 [49–69]	<0.01
Systolic blood pressure (mmHg)	118 [105–130]	117 [100–133]	119 [109–130]	0.56
Heart rate (times/min)	76 [65–86]	79 [65–94]	72 [66–81]	0.02
Diabetes	63 (32.6)	39 (45.3)	24 (22.4)	<0.01
Hypertension	101 (52.3)	58 (67.4)	43 (40.2)	<0.01
Coronary heart disease	39 (20.2)	23 (26.7)	16 (14.9)	0.04
Stroke	35 (18.1)	26 (30.2)	9 (8.4)	<0.01
NT-proBNP (pg/mL)	1,754 [407–5,034]	4,799 [1,661–7,871]	708 [284–2,239]	<0.01
Total bilirubin (µmol/L)	16 [11–25.7]	15.4 [10.5–23.8]	17 [11.5–26]	0.29
Albumin (g/L)	38.7 [35–42.9]	36.9 [34.4–39.5]	41 [36.3–44]	<0.01
Serum creatinine (µmol/L)	88 [73–120]	125 [110–169]	76 [66–82]	<0.01
eGFR (mL/min/1.73 m <sup>2</sup> )	66 [36–92]	33 [20–47]	89 [74–101]	<0.01
K <sup>+</sup> (mmol/L)	4.1 [3.8–4.5]	4.3 [4.0–4.6]	4.0 [3.8–4.2]	<0.01
PLT (10 <sup>9</sup> /L)	201 [163–259]	189 [151–255]	207 [174–265]	0.17
Hb (g/L)	132 [114–145]	122 [102–139]	135 [122–152]	<0.01
WBC (10 <sup>9</sup> /L)	6.57 [5.45–8.28]	7.45 [5.76–8.49]	6.11 [5.4–7.88]	<0.01
NLR	3.07 [2.26–4.7]	3.7 [2.68–5.3]	2.54 [2.05–3.8]	<0.01
EF value (%)	40 [40–60]	40 [40-44]	40 [40–60]	0.01
ARB	79 (40.9)	20 (23.2)	59 (55.1)	<0.01
Loop diuretics	120 (62.2)	54 (62.8)	66 (61.7)	0.87
NYHA	3 [2–3]	3 [2–3]	3 [2–3]	<0.01

The data are expressed as the n (%) or median [IQR]. NT-proBNP, N-terminal pro-B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; PLT, platelet; Hb, hemoglobin; WBC, white blood cell; NLR, neutrophil to lymphocyte ratio; EF, ejection fraction; ARB, angiotensin receptor blocker; NYHA, New York Heart Association; IQR, interquartile range.

CHF included sex (male), hypertension, stroke, an advanced age, elevated serum potassium concentration, decreased serum albumin concentration, hemoglobin concentration, and LVEF. In addition, ARB application was associated with a reduced risk of kidney injury.

The patients included in this study all met the guidelines for the diagnosis of CHF (19), and patients with CKD were excluded. Kidney injury was observed in 44.5% of the patients at admission, which is consistent with Cardiorenal Syndrome (CRS), which is characterized by chronic abnormalities in heart function followed by kidney injury or dysfunction (23,24). The main pathophysiology of CRS type 2 is a decrease in cardiac output and effective circulating blood volume in patients with HF, which can result in renal hypoperfusion and further activate the reninangiotensin-aldosterone system axis, sympathetic nervous system, and arginine vasopressin secretion, which can result in fluid overload, increased preload, and the deterioration of cardiac and renal function (25). de Silva *et al.* (13) examined 1,216 patients with CHF in a prospective cohort study, and reported that 57% of the patients developed renal insufficiency during the study period, which is consistent with the data from our findings and previous evidence (14,26). More than half of patients with CHF have a significantly increased risk of renal insufficiency. Thus, the protection and maintenance of renal function in

### Journal of Thoracic Disease, Vol 15, No 7 July 2023

Table 2 Results of the	univariate and	multivariate	logistic	regression	analysis

Risk factors	Univariate analysis			Multivariate analysis				
	Coefficient	OR	95% CI	Р	Coefficient	OR	95% CI	Р
Male	0.32915	1.38	0.77–2.48	0.26	1.45877	4.30	1.72–10.7	0.001
Age (years)	0.045226	1.04	1.02-1.06	0.0001	0.037134	1.03	1.008–1.06	0.01
Hypertension	1.12592	3.08	1.70–5.58	0.0002	1.30548	3.68	1.64-8.29	0.001
Stroke	1.55149	4.71	2.07-10.7	0.0002	1.34207	3.82	1.25–11.6	0.01
Diabetes	1.05420	2.86	1.54–5.34	0.0009	-	-	-	-
Coronary heart disease	0.73063	2.07	1.01–4.24	0.04	-	-	-	-
ARB application	-1.40026	0.24	0.13-0.46	<0.01	-1.31291	0.26	0.11-0.61	0.001
Heart rate (times/min)	0.020186	1.02	1.003–1.03	0.02	-	-	-	-
NT-proBNP (pg/mL)	0.000050858	1.0001	1.00-1.0001	0.02	-	-	-	-
NLR	0.17718	1.19	1.06–1.33	0.002	-	-	-	-
Albumin (g/L)	-0.13345	0.87	0.82-0.93	<0.01	-0.11743	0.88	0.81–0.96	0.005
Hemoglobin (g/L)	-0.023577	0.97	0.96-0.98	0.0002	-0.024259	0.97	0.95–0.99	0.006
Serum potassium (mmol/L)	1.14499	3.14	1.65–5.96	0.01	1.30930	3.70	1.58-8.67	0.002
EF value (%)	-0.028373	0.97	0.94–0.99	0.03	-0.046991	0.95	0.92-0.98	0.01
NYHA grading	0.51469	1.67	1.10–2.53	0.01	-	-	-	_

ARB, angiotensin receptor blocker; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NLR, neutrophil to lymphocyte ratio; EF, ejection fraction; NYHA, New York Heart Association; OR, odds ratio; CI, confidence interval.

Table 3 Results	of the multivariate	e analysis after	adjustment for	confounders

Risk factors	Coefficient	OR	95% CI	Р
Male	1.70472	5.49	2.02–14.9	0.0008
Age (years)	0.037332	1.03	1.005–1.07	0.02
Hypertension	1.48744	4.42	1.71–11.43	0.002
Stroke	1.89892	6.67	1.80–24.6	0.004
ARB application	-1.26322	0.28	0.11-0.71	0.007
Albumin (g/L)	-0.11174	0.89	0.81-0.98	0.01
Hemoglobin (g/L)	-0.024466	0.97	0.95–0.99	0.008
Serum potassium (mmol/L)	1.51178	4.53	1.76–11.6	0.001
EF value (%)	-0.035670	0.96	0.92-1.004	0.08

ARB, angiotensin receptor blocker; EF, ejection fraction; OR, odds ratio; CI, confidence interval.

the treatment regimen of HF patients is of great clinical significance.

The multivariate regression analysis in this study showed that for each additional year of age, the risk of renal insufficiency increased by 3% in patients with CHF, which is consistent with previous reports (26). It may be that an increasing age is strongly associated with a decrease in the GFR mechanisms, including a decrease in the number and size of nephrons, glomerulosclerosis, tubulointerstitial fibrosis, and microvascular insufficiency (27). In relation to

the demographic characteristics of the patients, in addition to age, sex was also associated with the kidney injury, and our results suggest that men have a 4.3-fold higher risk of developing kidney injury than women. This is consistent with the findings of Fu *et al.* (28). Further research on the mechanism underlying the effect of gender on the kidney function in patients with CHF should be conducted.

In a cross-sectional study in which 74 patients with CHF were admitted consecutively, Jingi *et al.* (29) showed that hypertensive disease (OR: 3.1, 95% CI: 1.2–8.4) was an independent risk factor for the development of renal insufficiency. This is consistent with our findings and suggests that comorbid hypertensive disease leads to a 2–3-fold increase in the risk of renal insufficiency in patients with CHF.

In a retrospective cohort study of 289 patients with acute decompensated HF, Eren *et al.* (30) showed that the decreased hemoglobin level (OR: 0.684, 95% CI: 0.53–0.88) was an independent risk factor for kidney injury. In our study, the risk of kidney injury was reduced by 3% for every 1 g/L increase in hemoglobin. The above evidence indicated that there was a negative correlation between hemoglobin concentration and renal function in patients with heart failure. Possible mechanisms included anemia or decreased hemoglobin concentration which may lead to renal ischemia and hypoxia (31,32).

Patients with stroke have a significantly increased risk of renal injury (9.6%, 95% CI: 8.3–11.0%) due to volume depletion, iodine contrast use, or underlying medical conditions (33). Similarly, the findings of our multivariate analysis suggest that CHF stroke patients have a 3.8-fold risk of developing kidney injury compared to those without stroke.

ARB drugs are one of the four essential drugs recommended by the 2022 American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America (HFSA) guidelines that can significantly improve the cardiac function and prognosis of patients with HF (34). The use of ARB drugs in patients with HF in China is relatively common. However, HF patients with the kidney injury should theoretically discontinue or reduce the dose of ARBs because they reduce the pressure in the afferent arterioles, which further reduces the GFR, which leads to further kidney injury (35). However, a recent study showed that there was no significant difference in the kidney function between the acute CRS patients who discontinued and continued ARB use (36). In addition, patients who continued angiotensinconverting enzyme (ACE) inhibitor/ARB therapy after the onset of kidney injury did not have a significantly increased risk of HF or show any further deterioration of kidney function compared to those who discontinued the drug (36). The above evidence suggests that ARB drugs may have some safety in CHF patients with the kidney injury; however, in such patients, serum potassium and renal function indicators need to be closely monitored. Interestingly, the ARBs provided renal protection (OR: 0.26, 95% CI: 0.11–0.61) in our study. It may be that ARBs indirectly maintain kidney function by improving heart function in patients with HF.

Serum albumin plays an important role in maintaining plasma colloidal osmolality, renal perfusion, and glomerular filtration. In a 2017 study by Takaya et al. (37), which included 231 patients with acute decompensated HF, the multivariate analysis showed that decreased serum albumin levels (defined as a decrease of  $\geq 3$  g/L) were an independent risk factor for the development of AKI (OR: 2.25, 95% CI: 1.15-4.49). Similarly, in our study, for every 1 g/L increase in serum albumin, the risk of kidney injury in patients with CHF decreased by 22%. It may be that there is a fluid transfer from the intravascular to interstitium when the serum albumin concentration decreases, which results in decreased renal perfusion. However, lower serum albumin could be a result of underlying conditions, such as poor nutritional status and lower functional status, rather than a causative factor for kidney injury.

Heart failure per se is also an important risk factor for kidney injury. Our study showed that for every 1% increase in the EF value, the risk of kidney injury was reduced by 5% in the patients with CHF. It may be that an increase in the EF increases the effective circulating blood volume and renal perfusion pressure, which in turn exerts a protective effect on renal function. In a 2019 study, 3,914 patients with heart failure were included. Compared to those with EF  $\geq$ 50%, those with EF <30% and EF 30–49% had a 1.32-fold (95% CI: 1.06–1.65) and 1.06-fold (95% CI: 0.87–1.28) increased risk of acute renal injury, respectively (38).

Renal hypoperfusion in HF leads to increased reninaldosterone, which results in increased sodium absorption by the proximal tubules, which in turn leads to increased potassium excretion (39). Another important factor in the elevated serum potassium in patients with HF is the use of ACEs/ARBs (40). The results of this study suggest that for every 1 mmol/L increase in potassium, the risk of renal function damage in patients with CHF increases 3.7 folds. However, renal function impairment can also cause elevated blood potassium. Prospective randomized controlled studies examining the causal relationship between elevated blood potassium and decreased renal function need to be conducted in the future.

Renal injury can significantly affect the prognosis of patients with CHF. Thus, it is of great clinical significance to accurately identify high-risk groups early to enable appropriate preventive and therapeutic measures to be implemented. According to the results of this study, renal function and other important indicators should be closely monitored in patients who are male, and those who have an advanced age, hypertension, stroke, hypoproteinemia, anemia, a decreased EF value, elevated serum potassium, or other underlying diseases. Moreover, in-time treatment measures should be implemented to protect heart and kidney function, which is likely to reduce the occurrence of renal function damage and adverse outcomes.

This study had several limitations. First, as an observational study, there is a risk of selectivity and information bias; however, the subjects were diagnosed using strict inclusion and exclusion criteria according to guidelines. In addition, the model for the confounding factors was corrected to improve the reliability of the results. Second, the causal relationship between the risk factor indicators and outcome indicators was not sufficiently strong. It may be that some factors influence each other; thus, the findings need to be further validated. Third, hard endpoints, such as survival outcomes, were not included in this study. There was also a lack of information on the treatments and preventive measures for kidney injury. More relevant information should be included in future studies.

#### Conclusions

More than half of the CHF patients developed kidney injury during hospitalization. The independent risk factors for kidney injury in patients with CHF included sex (male), hypertension, and stroke. Kidney injury was positively correlated with age and serum potassium, and negatively correlated with serum albumin concentration, hemoglobin concentration, LVEF, and ARB application.

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study complied with the provisions of the Declaration of Helsinki (as revised in 2013), and was approved by the Ethics Committee of Beijing Anzhen Hospital, Capital Medical University (No. KS2023001). All the patients signed the informed consent form.

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# 3942

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