

# Predictors of acute kidney injury in patients with acute decompensated heart failure in emergency departments in China

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## Abstract

**Objective:** This retrospective multicentre observational study was performed to assess the predictors of acute kidney injury (AKI) in patients with acute decompensated heart failure (ADHF) in emergency departments in China.

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**Methods:** In total, 1743 consecutive patients with ADHF were recruited from August 2017 to January 2018. Clinical characteristics and outcomes were compared between patients with and without AKI. Predictors of AKI occurrence and underdiagnosis were assessed in multivariate regression analyses.

**Results:** Of the 1743 patients, 593 (34.0%) had AKI. AKI was partly associated with short-term all-cause mortality and cost. Cardiovascular comorbidities such as coronary heart disease, diabetes mellitus, and hypertension remained significant predictors of AKI in the univariate analysis. AKI was significantly more likely to occur in patients with a lower arterial pH, lower albumin concentration, higher creatinine concentration, and higher N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration. Patients treated with inotropic agents were significantly more likely to develop AKI during their hospital stay.

**Conclusion:** This study suggests that cardiovascular comorbidities, arterial pH, the albumin concentration, the creatinine concentration, the NT-proBNP concentration, and use of inotropic agents are predictors of AKI in patients with ADHF.

### Keywords

Predictors, diagnosis, outcomes, acute kidney injury, acute decompensated heart failure, emergency department

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## Introduction

Acute decompensated heart failure (ADHF) is a growing global health problem affecting more than 26 million individuals worldwide.<sup>1</sup> Twenty to forty percent of patients with ADHF develop acute kidney injury (AKI), known as acute cardiorenal syndrome, which is associated with significant mortality.<sup>2,3</sup> In China, most patients with acute cardiorenal syndrome are treated in the emergency department (ED). However, the published data on acute cardiorenal syndrome are limited to small case series and single-centre studies,<sup>4,5</sup> and no data is available from EDs in China. We conducted a 28-centre retrospective cohort study to investigate the predictors, diagnosis, and outcomes of AKI in patients with ADHF in EDs in China. To the best of our knowledge, this multicentre study of EDs is the largest-sample study of this kind in this geographical region to date. The findings provide important insight into the present

situation of patients with ADHF who develop AKI in the emergency setting in China.

## Methods

### Study participants

We conducted a retrospective multicentre observational study of 28 tertiary hospitals throughout 11 provinces and municipalities in mainland China. Each ED had an average of 120,000 to 300,000 visits annually. The study complied with relevant EQUATOR Network guidelines (The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies<sup>34</sup>) and was approved by the institutional review board of Peking University Third Hospital and all participating hospitals (M2017166, Peking University Third Hospital Medical Science Research Ethics

Committee, Beijing, 19 July 2017). All participants provided written informed consent for the study.

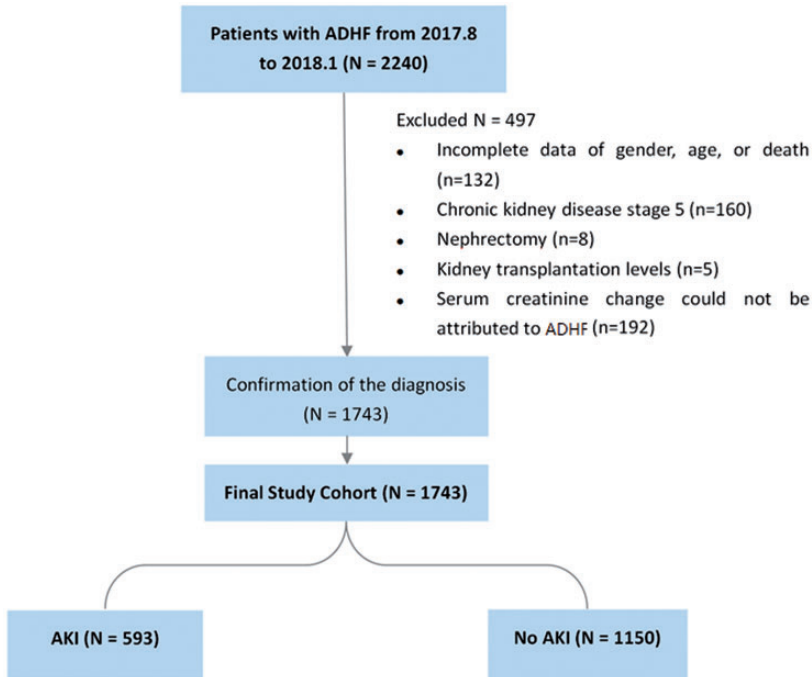
Adult patients (>18 years of age) with ADHF were consecutively enrolled from August 2017 to January 2018. All clinical data were collected from the electronic medical records. We de-identified the source data of all patients to ensure confidentiality. Data were manually entered via EpiData version 3.1 by dedicated research technicians. The patients' records were de-identified and independently reviewed by two senior ED physicians with >5 years of clinical experience (HX.G. and Y.L.) on a case-by-case basis to confirm the diagnosis of AKI according to the Kidney Disease: Improving Global Outcomes (KDIGO) definition<sup>7</sup> prior to analysis. Discrepancies between the reviewers were resolved through discussion. A third reviewer (QB.M.) was introduced if agreement was not reached after discussion. According to previous reports in the literature, the incidence of AKI in patients with ADHF is 29%.<sup>5</sup> The sample size was estimated using the formula for calculation of the sample size of cross-sectional studies; the allowable error was  $\pm 2\%$ , and  $\alpha = 0.05$  bilateral. The estimated sample size was 1978.

In total, 2240 patients with ADHF were initially enrolled in this study. Patients with incomplete data regarding sex, age, or clinical outcome ( $n = 132$ ) were excluded. Patients with a history of stage 5 chronic kidney disease (CKD) ( $n = 160$ ), nephrectomy ( $n = 8$ ), and kidney transplantation ( $n = 5$ ) were also excluded. Furthermore, because the aim of the study was to explore the interaction of ADHF and AKI, we excluded patients with AKI that was assumed to have been caused by drug toxicity, contrast medium, and confirmed severe sepsis; these patients were excluded because their serum creatinine change could not be definitively attributed to ADHF

( $n = 192$ ). Finally, the remaining 1743 participants were entered the final analysis (Figure 1).

### Definitions

ADHF was defined according to the definitions established in the 2013 American College of Cardiology Foundation/American Heart Association Guideline for the Management of Heart Failure.<sup>6</sup> AKI in patients with ADHF was diagnosed according to the 2012 KDIGO clinical practice guideline for AKI.<sup>7</sup> We used both creatinine and urine criteria if the source data were available in the electronic medical record. For patients whose urine data were missing, we used only creatinine criteria. According to the 2012 KDIGO clinical practice guidelines for AKI, patients were assumed to have a normal baseline creatinine concentration (estimated glomerular filtration rate (eGFR) of  $75 \text{ mL/min/1.73 m}^2$ ) when they had no history of CKD and unknown baseline kidney function. For patients with CKD and an unknown previous creatinine concentration, the diagnosis of AKI was mainly based on changes in the in-hospital serum creatinine concentration. The diagnosis of AKI was confirmed by the physicians' clinical judgements during the chart review. However, we also performed a software analysis through Python based on the same criteria. Non-recognition of AKI was defined as satisfaction of the diagnostic criteria for AKI that failed to be recognised by clinical doctors. Based on the related guidelines, CKD was defined in this study as an eGFR of  $<60 \text{ mL/min/1.73 m}^2$  for a 3-month duration. Hypertension was diagnosed by an increase in blood pressure exceeding 130/80 mmHg. Patients with hypertension were defined as those who had been diagnosed and required antihypertensive drugs. Coronary heart disease referred to coronary atherosclerotic heart



**Figure 1.** From August 2017 to January 2018, 2240 patients with ADHF were enrolled. We excluded 497 patients because of incomplete data regarding sex, age, or death (n = 132); a history of stage 5 chronic kidney disease (n = 160), nephrectomy (n = 8), or kidney transplantation (n = 5); and a serum creatinine change that could not be attributed to ADHF (n = 192). The final study population comprised 1743 patients with ADHF (593 with AKI and 1150 without AKI)

ADHF, acute decompensated heart failure; AKI, acute kidney injury.

disease. Patients with diabetes in this study were defined as those with a clear history of diabetes and long-term use of hypoglycaemic drugs. Considering the differences in blood lipid concentrations between Chinese and non-Chinese patients and based on the 2016 Chinese guidelines, hyperlipidaemia was diagnosed in patients with a total cholesterol concentration of >6.2 mmol/L, triglyceride concentration of >2.3 mmol/L, and low-density lipoprotein concentration of >4.1 mmol/L.

### Study endpoints

The primary endpoints for the short-term prognosis were 7-day all-cause mortality

and 30-day all-cause mortality. In-hospital all-cause mortality was also analysed and was calculated from arrival at the ED to hospital discharge. The secondary endpoints were the length of stay and the 30-day readmission rate. Emergency and hospitalisation cost data were collected from the financial department of each hospital and compared between patients with and without AKI. We also investigated predictors of the occurrence and underdiagnosis of AKI among patients with ADHF in the ED. The admission route for all patients was emergency admission followed by admission to the inpatient department for continuation of treatment. The data collected in this study began at the patient's

emergency visit and extended throughout the hospitalisation period.

### Statistical analysis

Quantitative variables were expressed as mean  $\pm$  standard deviation or median (25th–75th percentile) according to their distribution. The independent-samples Student's t test or the Mann–Whitney U test was used for continuous variables. Categorical variables were expressed as count and frequency. Comparisons between groups were performed using Pearson's chi-square test or Fisher's exact test. Variables were identified in the univariate analyses as those with a p-value of  $<0.05$  or those that were considered of clinical significance, including but not limited to age, sex, comorbidities, vital signs on arrival, arterial blood gas analysis, myocardial injury biomarkers, and use of inotropic agents. Collinearity was checked through Spearman's correlation analysis. Multivariable analyses were then performed using binary logistic regression. A multivariable formula was generated through backward stepwise selection by maximum likelihood estimation. All analyses were two-sided with a significance level of 0.05 and were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

## Results

### Baseline patient characteristics

The study population comprised 1743 patients with ADHF, 593 (34.0%) of whom had AKI. The patients' demographic and clinical characteristics are listed in Table 1. There were no significant differences in the age or sex composition between patients with and without AKI. Patients who developed AKI had a significantly higher rate of comorbidities, including

hypertension ( $p=0.001$ ), coronary artery disease ( $p=0.001$ ), diabetes mellitus ( $p=0.001$ ), hyperlipidaemia ( $p=0.011$ ), and CKD ( $p=0.001$ ), than patients without AKI. The heart rate was significantly higher in patients with than without AKI (98 vs. 91 bpm, respectively;  $p=0.003$ ). There were no significant differences in the systolic or mean blood pressure between patients with and without AKI. The arterial blood gas analysis showed that patients with AKI presented with a significantly lower arterial pH ( $p<0.001$ ), base excess ( $p<0.001$ ), and ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$  ratio) (i.e., oxygenation index) ( $p=0.001$ ) and a higher lactate concentration ( $p=0.007$ ) than patients without AKI. In the AKI group, the serum creatinine concentration, blood urea nitrogen (BUN) concentration, and BUN/creatinine ratio were higher in accordance with a lower eGFR ( $p<0.05$ ). There was no significant difference in vasodilator use during treatment between the two groups. Invasive ventilator therapy was administered to a higher proportion of patients with than without AKI (22.3% vs. 5.1%, respectively;  $p=0.001$ ). The 7-day all-cause mortality, 30-day all-cause mortality, and in-hospital all-cause mortality rates were significantly higher in patients with than without AKI ( $p<0.0001$  for all) (Figure 2).

*Multivariate predictors of AKI in patients with ADHF.* Given the significant differences in baseline characteristics between patients with and without AKI, a logistic regression model was used to adjust for potential confounders. Age, sex, cardiovascular comorbidities, arterial blood gas analysis, haemoglobin concentration, albumin concentration, creatinine concentration, BUN concentration, BUN/creatinine ratio, eGFR, troponin concentration, N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration, and use of inotropic agents

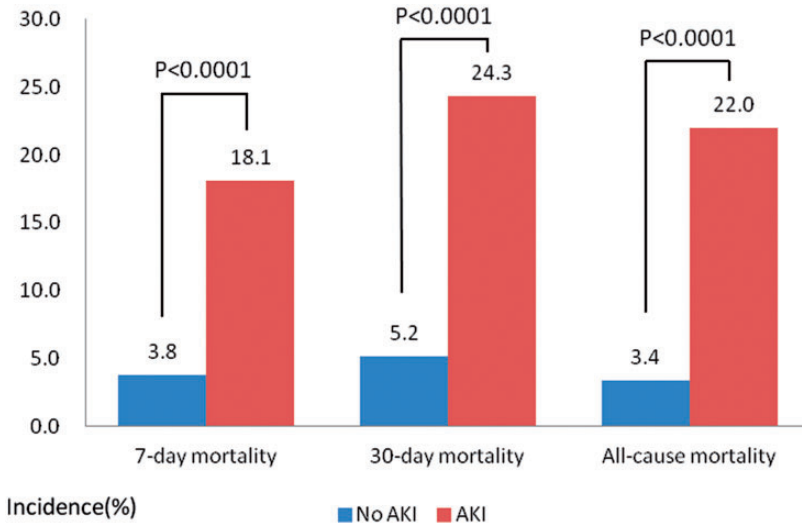
**Table 1.** Demographic and clinical characteristics of the study population

	Total (n = 1743)	Non-AKI (n = 1150)	AKI (n = 593)	p
<b>Demographics</b>				
Age, years	74 (63–82)	74 (63–82)	75 (63–84)	0.069
Male	687 (51.8)	496 (50.4)	191 (55.7)	0.103
<b>Comorbidities</b>				
Hypertension	853 (76.2)	611 (73.3)	242 (84.6)	0.001
Coronary heart disease	706 (68.5)	506 (65.1)	200 (78.7)	0.001
Diabetes mellitus	463 (48.7)	326 (45.5)	137 (58.5)	0.001
Hyperlipidaemia	157 (19.7)	108 (17.7)	49 (26.5)	0.011
COPD	164 (17.1)	108 (16.4)	56 (18.8)	0.530
CKD	74 (10.0)	39 (6.8)	35 (20.7)	0.001
<b>Vital signs</b>				
Heart rate, bpm	92 (78–112)	91 (78–110)	98 (80–117)	0.003
Systolic blood pressure, mmHg	138 (120–161)	138 (120–160)	140 (120–164)	0.250
Mean blood pressure, mmHg	99 (86–114)	99 (88–114)	98 (86–116)	0.677
<b>Laboratory values</b>				
pH	7.41 (7.34–7.45)	7.41 (7.36–7.45)	7.38 (7.30–7.44)	<0.001
pCO <sub>2</sub> , mmHg	36 (30–42)	36 (31–42)	34 (28–41)	<0.001
pO <sub>2</sub> , mmHg	80 (61–100)	80 (62–100)	78 (60–100)	0.440
Lactate, mmol/L	1.7 (1.1–2.7)	1.7 (1.1–2.5)	1.8 (1.2–3.2)	0.007
Base excess, mmol/L	−1.8 (−5.7 to 1.7)	−0.9 (−4.0 to 2.5)	−3.9 (−8.2 to −0.4)	<0.001
PaO <sub>2</sub> /FiO <sub>2</sub> ratio, mmHg	245.8 (186.1–334.8)	257 (196.2–343.8)	228.3 (164.2–307.7)	0.001
Sodium, mmol/L	138 (135–141)	138 (135–141)	137 (134–141)	0.012
NT-proBNP, pg/mL	4386 (1048–11635)	3435 (938–9000)	7690 (1299–21235)	<0.001
Troponin I, ng/mL	0.08 (0.03–0.50)	0.06 (0.03–0.46)	0.13 (0.04–0.63)	<0.001
Haemoglobin, g/L	120 (100–137)	123 (105–139)	112 (90–133)	<0.001
ALB, g/L	36.8 (33.0–40.0)	37.0 (33.1–40.0)	36.0 (32.0–40.0)	0.003
BUN, mg/dL	8.7 (6.05–14.6)	7.4 (5.6–10.7)	12.7 (8.1–21.2)	<0.001
BUN/Cr ratio	20 (15–26)	21 (16–27)	18 (13–24)	<0.001
Cr, mmol/L	99 (74–165)	85 (67–115)	164 (104–292)	<0.001
eGFR, mL/min/1.73 m <sup>2</sup>	47 (26–71)	57 (39–79)	27 (16–45)	<0.001
<b>Treatment</b>				
Invasive MV	72 (9.3)	30 (5.1)	42 (22.3)	0.001
Inotropic agent	145 (8.8)	62 (5.7)	83 (14.8)	<0.001
Vasodilators*	593 (79.9)	422 (71.0)	129 (70.5)	0.926
<b>Outcome</b>				
All-cause 7-day mortality	98 (7.4)	37 (3.8)	61 (18.1)	0.001
All-cause 30-day mortality	132 (10.1)	51 (5.2)	81 (24.3)	0.001
In-hospital all-cause mortality	100 (8.1)	31 (3.4)	69 (22.0)	0.001
Length of hospital stay, days	12.7 ± 32.2	11.64 ± 25.5	15.62 ± 46.4	0.606
30-day readmission	138 (10.8)	96 (10.1)	42 (12.7)	0.217
Cost*, ¥	14322 ± 19947	12092 ± 15767	18510 ± 25622	0.030

Data are presented as median (25th–75th percentiles), n (%), or mean ± standard deviation.

\*Number of patients with data was limited; for reference only.

AKI, acute kidney injury; ALB, serum albumin; BUN, blood urea nitrogen; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; Cr, creatinine; eGFR, estimated glomerular filtration rate; MV, mechanical ventilation; NT-proBNP, N-terminal pro-brain natriuretic peptide; PaO<sub>2</sub>/FiO<sub>2</sub> ratio, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (oxygenation index); pCO<sub>2</sub>, partial pressure of carbon dioxide; pO<sub>2</sub>, partial pressure of oxygen.



**Figure 2.** Incidence of ADHF with and without AKI in terms of 7-day mortality, 30-day mortality, and all-cause mortality  
ADHF, acute decompensated heart failure; AKI, acute kidney injury.

on arrival at the ED were recognised as significant predictive factors for AKI during the hospital stay ( $p < 0.05$ ). Furthermore, hypertension and coronary heart disease remained significant independent predictors of AKI, with adjusted odds ratios (ORs) of 1.771 and 1.543 ( $p = 0.008$  and  $0.018$ ), respectively). AKI was more likely to occur and develop in patients with a lower arterial pH, lower albumin concentration, and higher NT-proBNP concentration with ORs of 0.058, 0.966, and 1.202 ( $p = 0.002$ ,  $0.021$ , and  $0.009$ ), respectively. Patients treated with inotropic agents were more likely to develop AKI during their hospital stay (OR, 2.879;  $p < 0.001$ ) (Table 2).

### *Risk factors for underdiagnosis of AKI in patients with ADHF*

We recorded a very high rate of non-recognition of AKI by the physicians in the ED; the AKI in 318 (53.7%) of 593 patients with identifiable AKI remained unrecognised by the physicians in charge

in the ED. At the hospital level, 22 (78.5%) hospitals did not give a correct diagnosis of AKI. Twelve clinical characteristics were entered into multivariate logistic regression models to assess their possible predictive value for underdiagnosis of AKI. Among these variables, the  $\text{PaO}_2/\text{FiO}_2$  ratio (OR, 2.007; 95% confidence interval, 1.020–3.018;  $p = 0.001$ ) was the strongest predictor of missed diagnosis of AKI. A history of hypertension or diabetes mellitus markedly differed between the two groups ( $p = 0.007$ ), but neither was an independent risk factor for missed diagnosis of AKI (Tables 3 and 4).

## **Discussion**

### *Main findings*

The two major findings of the current investigation of EDs in China were that (1) hypertension, coronary artery disease, arterial pH, the albumin concentration, the creatinine concentration, the NT-proBNP concentration, and use of inotropic agents

**Table 2.** Independent predictors of acute kidney injury by multivariable logistic regression models.

Variable	Univariate				Multivariate			
	p-value	OR	95% CI		p-value	OR	95% CI	
Age (years)	0.184	1.148	0.936	1.408	0.226	1.009	0.994	1.024
Male sex	0.275	1.004	0.997	1.011	0.065	1.493	0.976	2.284
Hypertension	<0.001	2.026	1.514	2.711	0.008	1.771	1.162	2.699
Diabetes mellitus	<0.001	1.740	1.369	2.213	0.223	1.260	0.868	1.829
Coronary heart disease	0.001	1.526	1.184	1.968	0.018	1.543	1.078	2.209
Heart rate (bpm)	0.025	1.005	1.001	1.008	0.197	1.005	0.998	1.012
pH	<0.001	0.066	0.023	0.192	0.002	0.058	0.010	0.348
Haemoglobin (g/L)	<0.001	0.989	0.985	0.992	0.875	0.999	0.993	1.006
ALB (g/L)	<0.001	0.965	0.949	0.983	0.021	0.966	0.938	0.995
Cr ( $\mu$ mol/L)	<0.001	1.003	1.003	1.004	0.004	1.001	1.000	1.002
NT-proBNP/10,000 (pg/mL)	<0.001	1.373	1.244	1.515	0.009	1.202	1.047	1.380
Inotropic agent	<0.001	2.879	2.036	4.072	<0.001	0.233	0.127	0.428

ALB, serum albumin; CI, confidence interval; Cr, creatinine; NT-proBNP, N-terminal pro-brain natriuretic peptide; OR, odds ratio.

**Table 3.** Recognition of acute kidney injury by physicians in charge in emergency departments.

	Unrecognition of AKI	Recognition of AKI	p-value
Total (N = 593)	318 (53.7)	275 (46.3)	
Hospital level	22 (78.5)	6 (21.5)	0.001
PaO <sub>2</sub> /FiO <sub>2</sub> ratio, mmHg	271.1 ± 113.4	239.3 ± 110.6	0.004
Disease factors			0.007
Hypertension (n = 330)	169 (51.2)	161 (48.8)	
No hypertension (n = 105)	70 (66.7)	35 (33.3)	
Diabetes mellitus (n = 186)	95 (51.1)	91 (48.9)	
No diabetes mellitus (n = 187)	115 (61.5)	72 (38.5)	

Data are presented as n (%) or mean ± standard deviation.

AKI, acute kidney injury; PaO<sub>2</sub>/FiO<sub>2</sub> ratio, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (oxygenation index).

**Table 4.** Multivariable logistic regression analysis of failure to diagnose acute kidney injury

Variable	Failure to diagnose acute kidney injury			
	B	p-value	OR	95% CI
PaO <sub>2</sub> /FiO <sub>2</sub> ratio (mmHg)	0.002	0.001	2.007	1.020
Hypertension	-0.685	0.085	0.504	0.264
Diabetes mellitus	-0.179	0.141	0.836	0.427

CI, confidence interval; OR, odds ratio; PaO<sub>2</sub>/FiO<sub>2</sub> ratio, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (oxygenation index).



were likely to be the strongest predictors of AKI in patients with ADHF during their hospital stay and (2) the PaO<sub>2</sub>/FiO<sub>2</sub> ratio might be a predictor of failure to diagnose AKI in patients with ADHF.

### *ADHF with AKI and predictors*

The development of AKI in patients with ADHF has been an area of significant interest. Nonetheless, relevant information from EDs of developing countries is scarce. Our study showed that among EDs in China, about 34% of patients with ADHF had AKI, which was higher than the proportion of such patients in developed countries (29%).<sup>5</sup> Therefore, AKI in patients with ADHF is a burden for emergency physicians in China. In the present study, there was no significant difference in the age or sex composition between patients with and without AKI. The median age of the whole patient cohort was 74 years, which is similar to that in most studies of AKI in patients with heart failure.<sup>33</sup> As shown in previous studies, the patients in the current study presented with cardiovascular comorbidities such as hypertension, diabetes, hyperlipidaemia, and coronary heart disease, and patients with CKD were more likely to develop AKI.<sup>12–14,31,32</sup> A low arterial pH and base excess and a high lactate concentration indicate the presence of acidosis, which is closely associated with renal injury.<sup>28</sup> Moreover, invasive mechanical ventilation therapy and use of inotropic agents were more frequently observed in patients with ADHF who developed AKI, and both were significant indicators of critical illness as well as higher in-hospital mortality.<sup>29</sup> These findings are consistent with prior reports of hospitalised patients with ADHF.<sup>4,8–10</sup> Unfortunately, the complex pathophysiology of acute cardiorenal syndrome is still poorly understood and likely involves interrelated haemodynamic and neurohormonal mechanisms.<sup>9,11</sup> These

findings emphasise the need to identify modifiable predictors of AKI in patients with ADHF. In our study, hypertension, coronary artery disease, arterial pH, albumin, creatinine, NT-proBNP, and use of inotropic agents were likely to be the strongest predictors of AKI in patients with ADHF during their hospital stay. CKD was not included in the logistic regression for independent predictors in our study because of potential collinearity. However, several large-cohort studies have demonstrated that patients with AKI are also likely to have risk factors for CKD<sup>12–14</sup> and that patients with known background CKD are likely to develop AKI.<sup>15–17</sup> The reason for their mutual influence might be the close interactions among the underlying pathophysiology, pathology, definitions, and risk factors of the two conditions.<sup>18</sup> The economic impact of AKI in patients with ADHF was also noteworthy, although it was not the main purpose of this study. Our analysis demonstrated that AKI conferred a  $\geq 50\%$  increase in the costs of emergency care and hospitalisation.<sup>30</sup>

### *Underdiagnosis of AKI and independent risk factors*

The present study revealed an extremely high rate of AKI underdiagnosis among Chinese hospitals (78.5%). The underdiagnosis of AKI is the main contributor to the high mortality of patients with ADHF. In the ED, the condition of patients with ADHF is often critical and complicated by their older age and numerous underlying diseases. Prompt diagnosis and appropriate treatment for all diseases are needed to improve patients' outcomes.<sup>22</sup> ED physicians tend to pay more attention to the care of critically ill patients in urgent situations when enhanced computed tomography or medications that induce renal toxicity are inevitable for further diagnosis or treatment of these patients' primary

diseases, either ignoring the possibility of AKI or instituting such measures before acknowledging the occurrence of AKI. Thus, the diagnosis of AKI can be very challenging for ED physicians. In our study, the rate of missed diagnosis of AKI in patients with ADHF was as high as 53.7%, and the diagnosis tended to be missed in patients with a higher  $\text{PaO}_2/\text{FiO}_2$  ratio. Heart failure itself can cause increased pulmonary oedema, which decreases the  $\text{PaO}_2/\text{FiO}_2$  ratio and might partly represent the severity of heart failure. Both human and preclinical experimental studies have demonstrated a kidney–lung interaction in which AKI leads to lung injury and inflammation while acute lung injury with its attendant hypoxaemia may also worsen renal function.<sup>23–25</sup> Thus, ED physicians should be alert to the development of AKI in patients with ADHF, even if the  $\text{PaO}_2/\text{FiO}_2$  ratio is only slightly reduced. Moreover, patients without hypertension and diabetes mellitus are prone to be underdiagnosed. Awareness of these characteristics may help to recognise AKI. Further studies are needed to thoroughly assess the preventable causes and underdiagnosis of AKI in patients with ADHF.

### *Study limitations*

This study had several limitations. First, a considerable number of patients presented without data regarding their baseline creatinine concentration and urine volume. Moreover, some patients (although a minority) underwent repeated measurements of their serum creatinine concentration (more than twice). Therefore, the diagnosis of AKI might have been underestimated. However, we included all available information to reduce bias originating from establishment of the diagnosis, which was the basis of this study. Second, because this was a retrospective study, the data for several key indicators were missing; this

limited the sample size in the final logistic regression. Finally, the study was performed mainly in EDs of tertiary hospitals, which might have impacted the generalisability of the results to patients in community hospitals or other study settings. Despite these limitations, however, this study provides insight into the predictors and under-recognition of AKI in patients with ADHF in Chinese EDs.

### **Conclusions**

AKI might be partly associated with short-term mortality and cost in patients with ADHF in Chinese EDs. Cardiovascular comorbidities, arterial pH, albumin, creatinine, NT-proBNP, and use of inotropic agents are probably the strongest independent predictors of AKI in patients with ADHF. The  $\text{PaO}_2/\text{FiO}_2$  ratio is also a potential predictor of underdiagnosis of AKI. Further studies are needed to identify preventive and management strategies to reduce the burden of AKI in the ED.

### **Perspectives**

**Competency in Medical Knowledge:** Patients with concurrent ADHF and AKI might have higher mortality and increased medical costs. Cardiovascular comorbidities, arterial pH, albumin, creatinine, NT-proBNP, and use of inotropic agents could be significant risk factors for AKI in patients with ADHF. The rate of missed diagnosis of AKI is high among patients with ADHF. The  $\text{PaO}_2/\text{FiO}_2$  ratio may be a risk factor for underdiagnosis of AKI.

**Competency in Patient Care:** Patients with ADHF admitted to EDs should be monitored in terms of their urine output and serum creatinine concentration, and ED physicians should be alert to the occurrence of AKI.

**Translational Outlook 1:** This was a relatively short-term study (median of 3 months); therefore, longer-term follow-up of patients will lead to better identification of outcomes and underdiagnosis of AKI combined with ADHF.

**Translational Outlook 2:** Despite the quite sufficient sample size of this study and the difficulty in collecting emergency data, a larger sample size and more complete data from multiple hospitals in China might be helpful in detecting the risk factors for AKI and the underdiagnosis of AKI in patients with ADHF across China.

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