Original Paper

One-Year Survival and Renal Function Recovery of Acute Kidney Injury Patients with Chronic Heart Failure

Wen Zhang Dan Wen Yan-Fang Zou Ping-Yan Shen Yao-Wen Xu
Hao Shi Jing Xu Xiao-nong Chen Nan Chen

Department of Nephrology, Ruijin Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, PR China

Key Words

Acute kidney injury · Chronic heart failure · Prognosis

Abstract

Objective: To describe and analyze the clinical characteristics of acute kidney injury (AKI) patients with preexisting chronic heart failure (CHF) and to identify the prognostic factors of the 1-year outcome. **Methods:** A total of 120 patients with preexisting CHF who developed AKI between January 2005 and December 2010 were enrolled. CHF was diagnosed according to the European Society of Cardiology guidelines, and AKI was diagnosed using the RIFLE criteria. Clinical characteristics were recorded, and nonrecovery from kidney dysfunction as well as mortality were analyzed. **Results:** The median age of the patients was 70 years, and 58.33% were male. 60% of the patients had an advanced AKI stage ('failure') and 90% were classified as NYHA class III/IV. The 1-year mortality rate was 35%. 25.83% of the patients progressed to end-stage renal disease after 1 year. Hypertension, anemia, coronary atherosclerotic heart disease and chronic kidney disease were common comorbidities. Multiple organ dysfunction syndrome (MODS; OR, 35.950; 95% CI, 4.972–259.952), arrhythmia (OR, 13.461; 95% CI, 2.379–76.161), anemia (OR, 6.176; 95% CI, 1.172–32.544) and RIFLE category (OR, 5.353; 95% CI, 1.436–19.952) were identified as risk factors of 1-year mortality. For 1-year nonrecovery from kidney dysfunction, MODS (OR, 8.884; 95% CI, 2.535–31.135) and acute heart failure (OR, 3.281; 95% CI, 1.026–10.491) were independent risk factors. **Conclusion:** AKI patients with preexisting CHF were mainly elderly patients who had an advanced AKI stage and NYHA classification. Their 1-year mortality and nonrecovery from kidney dysfunction rates were high. Identifying risk factors may help to improve their outcome.

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W.Z. and D.W. contributed equally to this work.

Prof. Nan Chen
Department of Nephrology, Ruijin Hospital
School of Medicine, Shanghai Jiaotong University
No. 197 Ruijin Er Road, Shanghai 200025 (PR China)
E-Mail cnrj100@126.com

Introduction

Acute kidney injury (AKI) is a critical complication mainly found in patients in intensive care units. It is also complicated in patients with heart failure and closely associated with a poor outcome [1–5]. Chronic heart failure (CHF) is a critical health condition with a prevalence rate of 2–3% which rises in accordance with age [6]. Cardiac and renal dysfunction could be comorbidities of these patients, and may influence each other, worsen clinical outcomes and increase the burden of medical expenses. With the widening knowledge of the cardiorenal syndrome, interactions between kidney and heart that contribute to disease progression have received more and more attention. Apart from the current understanding of the diseases, there could be some other factors that may affect the outcome of those CHF patients who have experienced a ‘kidney attack’. Currently, most studies focus on the onset risk of AKI in the CHF population, while mortality as well as recovery from kidney dysfunction in this population was less discussed.

In the present study, clinical features of AKI patients with preexisting CHF were investigated, and prognostic factors for 1-year all-cause mortality and nonrecovery from renal dysfunction were studied.

Methods

This retrospective study was approved by the Ethics Committee of Ruijin Hospital affiliated to the Shanghai Jiaotong School of Medicine, Shanghai, PR China. Informed consent was obtained from all enrolled patients.

Participants and Criteria

Patients with preexisting CHF who developed AKI in the renal ward at our center between January 2005 and December 2010 were recruited. AKI was diagnosed using the RIFLE criteria proposed by the Acute Dialysis Quality Initiative Group [7]. The patients were classified into three severity categories (risk, injury and failure) and two clinical outcome categories [loss and end-stage renal disease (ESRD)]. ‘Risk’ was defined as an increase in the serum creatinine (SCr) level to ≥ 1.5 times that of the baseline value or a decrease in the estimated glomerular filtration rate (eGFR) of $\geq 25\%$; ‘injury’ was defined as an increase in the SCr level to ≥ 2.0 times that of the baseline value or a decrease in the eGFR of $\geq 50\%$; ‘failure’ was defined as an increase in SCr level to ≥ 3.0 times that of the baseline value or a decrease in the eGFR of $\geq 75\%$ or an absolute SCr level of ≥ 4 mg/dl with an acute rise of ≥ 0.5 mg/dl. The RIFLE classification was determined by the maximal SCr level during hospitalization. Baseline SCr values were acquired from the patients’ medical records stored in our electronic database, while for those for whom data were unavailable, the baseline SCr level was estimated by using the Modification of Diet in Renal Disease (MDRD) study equation [7].

CHF was diagnosed according to the medical history, clinical symptoms (decreased exercise tolerance or fluid retention) and laboratory examinations (chest X-ray, electrocardiography, specific biomarkers and echocardiogram) in accordance with the European Society of Cardiology (ESC) guidelines [6]. Based on the clinical manifestation, the NYHA classification was applied to evaluate cardiac function. Patients with AKI caused by acute heart failure (AHF) or acute coronary syndrome are defined as having cardiorenal syndrome (CRS) type 1, regardless of the presence of CHF or chronic kidney disease (CKD) [8, 9].

Patients aged <20 or >90 years, kidney transplant recipients and patients receiving dialysis were excluded. All the cases were strictly selected concurrently by two project investigators to ensure the accuracy of the inclusion criteria.

Data Collection

Basic data such as demographics, laboratory examinations, comorbidities and exposures were collected. All the laboratory indexes listed in table 1 were first detections after admission. Hypertension, chronic obstructive pulmonary disease, diabetes mellitus, anemia, stroke history, coronary atherosclerotic heart disease, malignant neoplasm and CKD that existed 3 months prior to the occurrence of AKI were recorded.

Table 1. Comparison of basic characteristics of AKI patients with CHF, grouped by 1-year survival

	Total (n = 120)	Survival (n = 78)	Death (n = 42)	p value
Age, years	70 (58–76)	68 (53–75)	73.5 (68–82)	0.0014
Male	70 (58.33)	53 (67.95)	17 (40.48)	0.0037
Obesity	3 (2.63)	2 (2.70)	1 (2.50)	1.0000*
Laboratory index ^a				
Creatinine, $\mu\text{mol/l}$	144.5 (100.5–329.5)	143.5 (92.0–406.0)	146.5 (103.0–311.0)	0.9956
Uric acid, $\mu\text{mol/l}$	438.98 $\pm$ 191.24	422.35 $\pm$ 175.83	476.08 $\pm$ 221.04	0.2362
BUN, mmol/l	12.2 (7.4–22.7)	11.8 (6.5–22.8)	12.3 (8.1–21.3)	0.7502
Total cholesterol, mmol/l	4.46 (3.53–6.60)	4.56 (3.62–5.43)	4.38 (3.48–7.02)	0.9940
Total triglyceride, mmol/l	1.88 (1.27–2.94)	1.77 (1.27–2.67)	1.94 (1.21–3.10)	0.8417
eGFR, ml/min/1.73 m^2	39.93 (14.94–64.54)	40.28 (16.67–62.20)	37.95 (11.52–64.66)	0.0212

Values are expressed as means $\pm$ SD, medians (ranges) or n (%). BUN = Blood urea nitrogen. * Fisher's exact test result. ^a First in-hospital laboratory test.

Exposures including electrolyte imbalance, infection, AHF, surgery, arrhythmia and multiple organ dysfunction syndrome (MODS) were collected in this study. The definitions of comorbidities and exposures are listed in online supplementary Appendix 1 (see www.karger.com/doi/10.1159/000369834 for all online suppl. material).

Endpoints

One-year all-cause mortality rate and nonrecovery from kidney dysfunction after diagnosis were defined as outcomes in the present study. Patients were followed up at an outpatient department or via telephone contact (records were collected in the electronic health system). One-year nonrecovery from kidney dysfunction was defined as dialysis dependency at 1 year [10]. Since renal replacement therapy during hospitalization was not only a kind of treatment but also a sign indicating the severity of the illness to some extent, it was regarded as a potential prognostic factor in our study but not a short-term outcome.

Statistical Analysis

Continuous variables distributed normally are expressed as means $\pm$ standard deviations, while medians and interquartile ranges are used for describing skewed ones. Categorical variables are given as frequencies and percentages. The two-sample Student t test or the Wilcoxon rank sum test were used to compare the difference in the sample mean, and the χ^2 test or Fisher's exact test were conducted for evaluating rate differences. The RIFLE classification was treated as an ordered variable and analyzed with the Cochran-Mantel-Haenszel χ^2 test. Statistical significance was defined as a p value < 0.05 (two-tailed).

The independent prognostic factors for 1-year mortality and nonrecovery from kidney dysfunction were assessed by stepwise multivariate logistic regression analysis. All variables were put in the model, and the significance level to enter and stay was set at 0.05. Both models were established with validation and satisfied the Hosmer and Lemeshow goodness-of-fit test. All statistical analyses were conducted using SAS version 8.02 (SAS Institute, Cary, N.C., USA).

Results

Demographic Characteristics and Clinical Features

A total of 120 patients were enrolled in the current study. The median age of our cohort was 70 years (range, 58–76), and 58.33% (70/120) of the patients were male. The cohort was divided into two groups based on the 1-year mortality rate of all the patients. The patients of the 'death group' were older ($p < 0.01$) and more of them were female ($p < 0.01$). Of all the laboratory indexes, only the eGFR was significantly lower in the death group than in the

Table 2. Comparison of comorbidity and exposure of AKI patients with CHF, grouped by 1-year survival

	Total (n = 120)	Survival (n = 78)	Death (n = 42)	p value
Comorbidity				
Hypertension	77 (64.17)	52 (66.67)	25 (59.92)	0.4364
Anemia	49 (40.83)	22 (28.21)	27 (64.29)	0.0001
CAD	47 (39.17)	32 (41.03)	15 (35.71)	0.5697
CKD	43 (35.83)	32 (41.03)	11 (26.19)	0.1060
COPD	34 (28.33)	18 (23.08)	16 (38.10)	0.0816
DM	25 (20.83)	14 (17.95)	11 (26.19)	0.2890
Stroke history	17 (14.17)	13 (16.67)	4 (9.52)	0.4119*
Malignant neoplasm	6 (5.00)	1 (1.28)	5 (11.90)	0.0196*
Exposures				
Electrolyte imbalance	97 (80.83)	59 (75.64)	38 (90.48)	0.0489
Infection	83 (69.17)	48 (61.54)	35 (83.33)	0.0137
AHF	49 (40.83)	26 (33.33)	23 (54.76)	0.0227
Surgery	38 (31.67)	27 (34.62)	11 (26.19)	0.3440
Arrhythmia	34 (28.33)	15 (19.23)	19 (45.24)	0.0026
MODS	28 (23.33)	5 (6.41)	23 (54.76)	<0.0001
Nephrotoxic agents	25 (20.83)	20 (25.64)	5 (11.90)	0.0772
Shock history	23 (19.17)	11 (14.10)	12 (28.57)	0.0548
Mechanical ventilation	12 (10.00)	2 (2.56)	10 (23.81)	0.0002*
AMI	11 (9.17)	8 (10.26)	3 (7.14)	0.7452*
RM	11 (9.17)	5 (6.41)	6 (14.29)	0.1539
Cerebral infarction	8 (6.67)	6 (7.69)	2 (4.76)	0.7116*
UGB	7 (5.83)	2 (2.56)	5 (11.90)	0.0503*
Sepsis	3 (2.50)	0	3 (7.14)	0.0409*

Values are n (%). CAD = Coronary atherosclerotic heart disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; AMI = acute myocardial infarction; RM = rhabdomyolysis; UGB = upper gastrointestinal bleeding. * Fisher's exact test result.

survival group ($p < 0.05$). The demographic information and laboratory examinations are listed in table 1.

Risk Factors for One-Year Mortality

As shown in table 2, anemia (28.21 vs. 64.29%, $p < 0.01$) and malignant neoplasm (1.28 vs. 11.90%, $p < 0.05$) were statistically different between the survival and the death group. Electrolyte imbalance ($p < 0.05$), AHF ($p < 0.05$), arrhythmia ($p < 0.01$), infection ($p < 0.05$), sepsis ($p < 0.05$), MODS ($p < 0.01$) and mechanical ventilation ($p < 0.01$) were proved to be risk factors for 1-year mortality without adjustment.

Table 3 showed the relationship between the RIFLE/NYHA classification and the 1-year outcome: 22.5% (27/120) of the patients were classified as belonging to the 'risk' group, 17.5% (21/120) as 'injury', and 60% (72/120) as 'failure'. The outcome of the patients worsened as the AKI stage advanced ($p < 0.01$); 10% (12/120) of the patients were classified into NYHA class I/II, and 90% (108/120) into class III/IV. However, there was no difference in the 1-year mortality rate and nonrecovery from kidney dysfunction between the two groups.

Taking into account that the onset of the CRS often indicates a poor prognosis, the outcome was compared between the CRS type 1 patients and non-CRS type 1 patients in the current study. However, there was no difference in 1-year outcome between the CRS type 1 and non-CRS type 1 patients (table 4).

Table 3. Comparison of 1-year outcome of AKI patients with CHF, grouped by different classifications

	Total (n = 120)	Risk (n = 27)	Injury (n = 21)	Failure (n = 72)	p value	NYHA I/II (n = 12)	NYHA III/IV (n = 108)	p value
Mortality (1-year)	42 (35.00)	2 (7.41) ^a	4 (19.05)	36 (50.00) ^b	<0.0001	3 (25.00)	39 (36.11)	0.5379*
Nonrecovery from kidney dysfunction (1-year)	31 (25.83)	1 (3.70) ^c	5 (23.81)	25 (34.72)	0.0019	3 (25.00)	28 (25.93)	1.0000*

Figures are n (%). * Fisher's exact test result. ^a Significant difference in 1-year mortality rate between 'risk' and 'failure'. ^b Significant difference in 1-year mortality rate between 'injury' and 'failure'. ^c Significant difference in 1-year nonrecovery from kidney dysfunction between 'risk' and 'failure'.

Table 4. Comparison of 1-year outcome of AKI patients with CHF, grouped by the presence of CRS type 1

	Total (n = 120)	Non-CRS type 1 (n = 63)	CRS type 1 (n = 57) ^a		p value*
			AHF (n = 49)	AMI (n = 11)	
Mortality (1-year)	42 (35.00)	18 (28.57)	23 (46.94)	3 (27.27)	0.1206
Nonrecovery from kidney dysfunction (1-year)	31 (25.83)	12 (19.05)	17 (34.69)	4 (36.36)	0.0742

Figures are n (%). AMI = Acute myocardial infarction. * p value of the χ^2 test between the groups of CRS type 1 and non-CRS type 1. ^a 57 cases of CRS type 1 included 49 cases with AHF and 11 cases with AMI, of which 3 patients had AHF and AMI while AHF was induced by AMI.

Table 5. Multivariate logistic regression analysis: independent risk factors for 1-year outcome

	One-year all-cause mortality ^a				One-year nonrecovery from kidney dysfunction ^b			
	Wald χ^2	OR	95% CI	p value	Wald χ^2	OR	95% CI	p value
MODS	12.5939	35.950	4.972–259.952	0.0004	11.6540	8.884	2.535–31.135	0.0006
Arrhythmia	8.6450	13.461	2.379–76.161	0.0033	–	–	–	–
Anemia	4.6106	6.176	1.172–32.544	0.0318	–	–	–	–
RIFLE category	6.2473	5.353	1.436–19.952	0.0124	–	–	–	–
AHF	–	–	–	–	4.0121	3.281	1.026–10.491	0.0452

^a Hosmer and Lemeshow goodness-of-fit test: χ^2 value = 3.8663, p = 0.7950. ^b Hosmer and Lemeshow goodness-of-fit test: χ^2 value = 1.4598, p = 0.4819.

Outcome and Logistic Regression Analysis

One-year outcomes are listed in tables 3 and 4. In our population, the 1-year all-cause mortality rate was 35% (42/120), and 25.83% (31/120) of the patients progressed to ESRD and depended on dialysis. All the variables recorded in tables 1–3 were put into a logistic regression model.

There were 4 risk factors for 1-year all-cause mortality in AKI patients with preexisting CHF. MODS was confirmed as the most significant risk factor (OR, 35.950; 95% CI, 4.972–259.952), followed by arrhythmia (OR, 13.461; 95% CI, 2.379–76.161), anemia (OR, 6.176; 95% CI, 1.172–32.544) and RIFLE classification (OR, 5.353; 95% CI, 1.436–19.952). For

1-year renal outcome, patients exposed to MODS (OR, 8.884; 95% CI, 2.535–31.135) and AHF (OR, 3.281; 95% CI, 1.026–10.491) were more likely to progress to ESRD. Detailed results of the multivariate logistic regression analysis are presented in table 5.

Discussion

Previous studies have reported that 13–36% of CHF patients had worsening renal function (WRF) [11–13], which was much higher than the AKI incidence among the total inpatients (3.2–9.6%) [14], indicating that the preexisting CHF may increase the incidence of WRF in hospitalized patients. Furthermore, evidence suggested that AKI or WRF in CHF patients was associated with poor prognosis [11] and an increased risk of readmission [15]. Therefore, current efforts to explore factors that are responsible for the outcomes of this cohort are warranted.

This study found that elderly males constituted the majority of our patients. The median age of all patients in our cohort was similar to that in the studies reported by Damman et al. [16] and Eren et al. [17]. Male patients made up the majority in our study, but female patients were predominant in the ‘death group’, which was consistent with the mortality rate in the heart failure population [18]. Besides age and sex, the eGFR was another factor that was statistically significant among the general characteristics. Hillege et al. [4] found that the eGFR was a more powerful tool than NYHA classification or left ventricular ejection fraction in predicting the mortality of patients. In our study, neither eGFR nor NYHA classification was a predictor after multivariate adjustment. One possible explanation is that the eGFR in our study was estimated by the SCr level after hospitalization and not the actual baseline SCr. Furthermore, the NYHA class III/IV group included much more patients than the NYHA class I/II group, which might also contribute to this result.

Our study had a higher mortality rate (35%) than those reported in the heart failure population (22%) [19] or the AKI population (20%) [20], as 60% of the patients in our study reached the ‘failure’ stage of AKI (otherwise reported as 22%) [12] and 90% patients were classified as NYHA class III/IV (otherwise reported as 37–90.1%) [3, 16]. 25.83% of the patients in our study progressed to ESRD and depended on dialysis, this rate being much higher than that found among the general population of AKI patients (about 5%) [21].

In accordance with the clinical features of heart failure patients [6], the common comorbidities in this study included hypertension, anemia, coronary atherosclerotic heart disease and CKD. In our study, 40.83% of the patients had anemia, which was higher than the rate among CHF patients (about 20%) [22]. Such a high rate of anemia might be due to a high rate of coexisting CKD in our patients. Furthermore, anemia was also an independent risk factor for 1-year mortality in our study. Most studies in the literature indicate that anemia is associated with an increased risk of mortality in both systolic and diastolic CHF [22] as well as in CKD [23] and CRS patients [24]. Meanwhile, patients with prior CKD [25] and preexisting CHF both have a high risk of developing AKI. Therefore, a close relationship was more likely to be found between AKI, CHF, CKD and anemia.

Among exposures, arrhythmia was an independent risk factor for 1-year mortality, with an incidence of 28.33% in our study. Cleland [26] also reported that arrhythmia was associated with increased mortality in CHF patients, with an incidence of 23%. As arrhythmia occurred in critical clinical situations such as CHF and AKI, the clinical value of arrhythmia was significant. AKI caused by AHF or acute myocardial infarction is a kind of CRS type 1, which was also an important exposure in our study. The occurrence of CRS type 1 (47.5%, 57/120 patients) in this study was higher than that in acute decompensated heart failure (ADHF) patients (25–33%) [9], and the 1-year mortality rate of CRS type 1 patients in our study, which was almost 1.5 times that of the non-CRS type 1 group, was much higher than that reported by

Gigante et al. [27]. The difference may be related to the fact that our patients had more comorbidities or exposures, since, in the overall population, a preexisting chronic heart dysfunction was found. In our research, AHF was an independent risk predictor of 1-year nonrecovery from kidney dysfunction rather than mortality, which may be due to irreversible damage to the kidney but timely diagnosis and treatment of AHF. In the exposures, MODS was found to be the most powerful independent risk factor for both 1-year mortality and nonrecovery from kidney dysfunction in our cohort. Although MODS has a high mortality rate itself, previous studies indicated that AKI and other organ failure were usually each other's prerequisites [28]. The cross talk between different organs could aggravate the disease, which is urging clinicians to remain alert to CRS, MODS and other critical clinical situations.

RIFLE and NYHA classifications are associated with clinical outcomes as reported in Cleland et al. [29]. However, only the RIFLE classification was an independent risk factor for 1-year all-cause mortality in our study. This inconsistency could be traced to the natural sample bias, since 90% of the patients in our population were classified into NYHA class III/IV. Hillege et al. [4] indicated that renal function, rather than NYHA classification, may be more likely to be a predictor of mortality in CHF patients with renal dysfunction, and Roy et al. [30] found that the application of the RIFLE criteria could increase the ability to predict adverse events compared to other AKI classifications (AKIN and KDIGO). Further investigation on the prognostic evaluation in this cohort is needed.

Our study also has some limitations. As a retrospective single-center study, a potential bias may exist. Data, such as systolic or diastolic pressure and left ventricular systolic function status, were incomplete and discarded, and the real GFR was unavailable and replaced by the eGFR.

In conclusion, CHF patients who suffered AKI in this study were mainly elderly males, and most patients had an advanced AKI stage and NYHA classification. The 1-year mortality and nonrecovery from kidney dysfunction rates were high. MODS, arrhythmia, anemia and RIFLE category were independent risk factors for 1-year all-cause mortality. AHF and MODS were independent risk factors for nonrecovery from kidney dysfunction. Our results illustrate the necessity of an early diagnosis and adequate classification of these patients to improve their outcome.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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