Original Article

Predicting the in-Hospital Outcome in Acute Heart Failure: Role of Laboratory Tests

Ekhlas Torfi[1], MD; Nasim Naderi[2], MD; Sepideh Taghavi[2], MD; Soodeh Omidi[3], PhD; Ahmad Amin[2*], MD

ABSTRACT

Background: Despite impressive advances in therapeutics in the last years, acute heart failure (AHF) remains a major cause of cardiovascular morbidity and mortality. Additionally, worsening renal failure (WRF) during hospitalization has a significant effect on rehospitalization and mortality in such patients. In this study, we aimed to determine the factors impacting on WRF and in-hospital mortality in patients with AHF.

Methods: During a 9-month period (September 2016 to May 2017), 104 patients with an episode of AHF (mean age: 75 y) were included in this study. The effects of demographic, echocardiographic, and laboratory findings on WRF and in-hospital outcomes (mortality and urgent heart transplantation) were evaluated retrospectively.

Results: Out of the 104 patients, 44.3% developed WRF; the incidence of in-hospital mortality and heart transplantation was 13.4%. Among the laboratory parameters, the specific gravity of urine was significantly associated with WRF (P = 0.03), and higher blood uric acid levels (P = 0.01) and lower left ventricular ejection fractions (P = 0.04) were associated with adverse in-hospital outcomes. Additionally, low hemoglobin (P = 0.03), high pro-BNP (P = 0.05), and low left ventricular ejection fractions (P = 0.04) were associated with a prolonged in-hospital stay.

Conclusions: Laboratory data can be used upon patient admission to guide the therapy of heart failure in an attempt to reduce WRF and in-hospital stay. ***(Iranian Heart Journal 2019; 20(3): 60-65)***

KEYWORDS: Acute heart failure, Outcome, Laboratory tests

[1] Atherosclerosis Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, IR Iran.
[2] Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[3] Department of Genetics, Faculty of Advanced Medical Technologies, Golestan University of Medical Sciences, Gorgan, IR Iran.

***Correspond Author:** Ahmad Amin, MD; Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Science, Tehran, IR Iran.
Email: amina33@gmail.com **Tell:** 09163050683

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Heart failure (HF) is a clinical syndrome resulting from a structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood commensurate with the needs of the body, or that precludes it from doing so in the absence of increased filling pressure. A cardinal manifestation of HF is fluid retention and fluid accumulation that cause congestion in the lungs, liver, intestines, and peripheral compartments.

Acute heart failure (AHF) is defined as the rapid or gradual onset of the signs and symptoms of heart failure that result in urgent

unplanned hospitalization or office or emergency department visits.

Despite advances in therapeutics, AHF remains a major cause of cardiovascular mortality and morbidity. Patients hospitalized because of AHF represent a high-risk population with limited short-term prognoses. A substantial component of AHF-related mortality occurs during the hospital stay. [1-2]

One of the most important issues in the AHF domain is worsening renal failure (WRF), defined as an absolute increase in serum creatine (Cr) (≥ 0.3 mg/dL from baseline) during the management of AHF. It has been reported that WRF is associated with an increased risk of short- and long-term mortality as well as a prolonged hospital stay and increased readmissions. [4-8] therefore, there is a need to better characterize and understand factors related to WRF and poor in-hospital outcomes in AHF.

The aim of the present study was to determine the correlation between several laboratory and echocardiographic parameters and WRF and their impact on the in-hospital outcome.

METHODS

This study was a single-center, prospective, observational, hospital-based study of patients admitted with AHF in Rajaie Cardiovascular, Medical, and Research Center (a tertiary center for AHF and transplantation programs in Tehran, Iran).

The patients were enrolled over a 9-month period, from September 2016 to May 2017. The inclusion criteria were comprised of age above 18 years, signs and symptoms of new-onset or worsening HF according to the accepted guidelines (based on clinical manifestations, chest X-ray, echocardiography, and NT pro-BNP), and plasma creatinine at the time of admission < 2 mg/dL (mg/d). The exclusion criteria consisted of patients with the acute coronary syndrome and cardiogenic shock, patients who had taken nephrotoxic drugs in the last 2 days, patients with high cardiac output cardiac failure, and patients undergoing chemotherapy.

The study data were collected on admission and throughout the hospital course. During admission, a comprehensive medical and drug history was taken and thorough physical examinations and echocardiographic examinations were performed by expert cardiologists.

Laboratory data—including complete blood count (CBC), blood sugar, blood urea nitrogen (BUN), serum Cr, sodium (Na), potassium (K), magnesium (Mg), liver enzymes, bilirubin, thyroid function, urine specific gravity, the iron profile (SI, TIBC, and ferritin), serum albumin and protein, uric acid, and NT-pro-BNP—were recorded on admission.

BUN and Cr levels were recorded on a daily basis until the discharge day.

Echocardiographic data—including the left ventricular size and function, the right ventricular size and function, the tricuspid regurgitation severity, the tricuspid regurgitant velocity, and the pulmonary artery pressure—were obtained by trained cardiologists.

Definitions

AHF was defined as a rapid or gradual onset of the signs and symptoms of HF resulting in urgent unplanned hospitalization or emergency department visits. WRF was defined as a minimum increase in serum creatinine of 0.3 mg/d to day 5. [6]

Study End Points

The primary end points were the relationship between laboratory test results and WRF or in-hospital mortality / urgent heart transplantation. The secondary end points were the relationship between echocardiographic data and WRF or in-hospital mortality / urgent heart transplantation.

Statistical Analysis

The statistical analyses were conducted SASS 15 statistical software for Windows (SPSS Inc,

Chicago, Illinois). The mean and standard deviations or the geometric mean and 95% confidence intervals were presented for the continuous variables and absolute and relative frequencies for the categorical variables.

For the evaluation of the distribution of data, the one-sample Kolmogorov–Smirnov test was used. Comparisons of the mean of the variables between 2 groups were performed via the independent *t*-test or the Man–Whitney *U*-test. The qualitative data were compared using the χ^2 test or the Kruskal–Wallis test (ordinal variables). A *P* value < 0.05 was considered statistically significant.

RESULTS

Over a 9-month period, 104 patients with AHF who met the inclusion criteria were included in this study. The mean age of these patients was 53 years; the patients were between the ages of 17 and 85 years. Laboratory parameters and echocardiographic data related to WRF, hospitalization, need for cardiac transplantation, and the rate of mortality were investigated. Seven patients were lost during follow-up. Based on the WRF defining criteria, in our study during hospitalization, the incidence of WRF was 44.3%. Seven (6.7%) patients died during the study, and 7 patients underwent heart transplantation (6.7%). The total rate of transplantation and mortality was estimated at 13.4%.

In-hospital stay was significantly longer in the AHF patients with WRF than in those without WRF (*P* = 0.001). Additionally, the patients who underwent heart transplantation and those who died had longer in-hospital stay durations than did the others (*P* = 0.04) (Table 1).

Table 1. Mean duration of in-hospital stay in the patients with and without WRF, with and without adverse in-hospital outcomes (mortality and urgent heart transplantation)

			Mean	*P* value
Hospitalization	WRF	Yes	13.6	0.001
		No	9.4	
	Mortality + Transplantation	Yes	16.1	0.049
		No	9.8	

WRF, Worsening renal failure

Among the laboratory parameters, the specific gravity of urine was significantly correlated with WRF (*P* = 0.03); nevertheless, no significant relationship was found between the other variables and WRF occurrence (*P* > 0.05) (Table 2).

Table 2. Relationship between multiple laboratory data and the development of WRF in the AHF patients

Variable	WRF		*P* value
	Yes	No	
Age (y)	52.69	53.35	0.95
Urine specific gravity	1.012	1.018	0.038
Pro-BNP (pg/mL)	6398.46	7380.55	0.71
Hb (gr/dL)	12.66	12.75	0.71
Na (MEq/L)	136.55	135.50	0.47
Fe (micg/dL)	51.78	64.31	0.34
TIBC (micg/dL)	275.54	273.78	0.84
LVEF (%)	17.20	20.19	0.10
SPAP (mmHg)	48.88	46.45	0.21
Protein (g/L)	67.18	66.34	0.97
Ferritin (ng/dL)	237.19	192.00	0.24
Albumin (g/L)	41.78	43.05	0.48
Uric acid (mg/dL)	9.07	8.47	0.15
Abnormal TFT	6 (14%)	7 (13%)	0.88
Abnormal LFT	22 (51.2%)	27 (50%)	0.90

WRF, Worsening renal failure; AHF, Acute heart failure; SPAP, Systolic pulmonary pressure; TIBC, Total iron-binding capacity

Among the laboratory parameters, cardiac parameters and high concentrations of uric acid in the serum had a significant relationship with mortality and heart transplantation (P = 0.01). The patients who died or received heart transplantation had a significantly lower left ventricular ejection fraction (LVEF) (P = 0.04) and were younger (P < 0.001) (Table 3).

Table 3. Relationship between multiple laboratory data and adverse in-hospital outcomes (mortality and urgent heart transplantation) in the AHF patients

	Mortality and Transplant		*P* value
	Yes	No	
Age (y)	39.85	55.64	<0.001
Urine specific gravity	1.01	1.01	0.78
Pro-BNP (pg/mL)	9362.66	6389.76	0.12
Hb (gr/dl)	12.97	12.79	0.84
Na (MEq/L)	133.64	136.38	0.07
Fe (micg/dL)	51.66	60.07	0.66
TIBC (micg/dl)	285.44	272.85	0.29
LVEF	13.46	19.60	0.04
SPAP	46.33	48.04	0.71
Protein(g/l)	65.09	67.20	0.79
Ferritin (ng/dl)	294.66	214.36	0.06
Albumin (g/l)	41.27	42.89	0.31
Uric acid (mg/dl)	9.97	8.34	0.01
Abnormal TFT	2 (14.3%)	11 (12.2%)	0.82
Abnormal LFT	9 (64.3%)	42 (46.7%)	0.22

WRF, Worsening renal failure; AHF, Acute heart failure; SPAP, Systolic pulmonary pressure; TIBC, Total iron-binding capacity

Lower hemoglobin (P = 0.003) and high pro-BNP (P = 0.05) were seen in the patients who had longer in-hospital stay durations. A lower LVEF had a significant correlation with a prolonged hospitalization course (P = 0.02) (Table 4).

Table 4. Relation coefficient between laboratory parameters and the in-hospital stay duration

	Relation Coefficient	*P* value
Age	- 0.1	0.07
Urine specific gravity	0.1	0.2
Pro-BNP	0.2	0.05
Hb	- 0.2	0.003
Na	- 0.2	0.1
Fe	- 0.07	0.5
TIBC	- 0.007	0.9
LVEF	- 0.23	0.02
SPAP	- 0.09	0.4
Protein	- 0.1	0.4

TIBC, Total iron-binding capacity; SPAP, Systolic pulmonary pressure; LVEF, Left ventricular ejection fraction

DISCUSSION

The LVEF is routinely measured in patients with HF. Changes in this cardiac parameter predict both mortality and the length of hospitalization. A reduced LVEF is a prognostic factor in HF patients. Previous studies have demonstrated that an improvement in the LV remodeling is associated with improved survival and reduced HF hospitalizations. It is recommended that the measurement of the LVEF be repeated in patients with clinical changes. [3] The results of previous studies have also demonstrated that patients with a lower LVEF have a greater risk of developing HF. [1, 6, 8]

In our study, we observed that the LVEF was a prognostic factor insofar as mortality occurred more frequently in the patients with a lower LVEF. We also observed the need for urgent

heart transplantation more frequently in the patients with a lower LVEF. Thus, our results confirm those reported by previous studies.

Previous research has demonstrated that the majority of patients with HF are old, which is because of the aging of populations in many countries and improvements in health care services for these patients. [10, 11] Some studies have shown that age is a prognostic factor for mortality in HF, whereas some others have not confirmed this hypothesis. Therefore, the role of age as a prognostic factor in mortality due to HF is not clear. In our study, mortality and heart transplantation rates among the younger patients were more than those of the older patients. Hence, our study probably demonstrated the role of age as a prognostic factor.

Urine specific gravity is a test to compare the density of urine and the density of water. [12] In other words, urine specific gravity is the ability of the kidney to concentrate urine. The normal range of this test is from 1.005 to 1.025 with a normal fluid intake. Urine specific gravity depends on the number and size of the compounds that are dissolved in urine. When the renal function decreases, an excreted body fluid rate < 80% leads to an increase in the urine specific gravity rate. This condition can occur in patients with HF. [13] Accordingly, the significant relationship between the rise in urine specific gravity and WRF in the patients with AHF in our study can be justified and the increase in urine specific gravity can be employed as a predictive factor for the development of WRF in such patients. Previous studies have shown that WRF has a negative effect on the outcome of patients suffering from HF. [14] Therefore, the determination of the predictive factors in WRF plays an important role in the management and treatment of these patients.

Some other laboratory parameters in our study are worthy of special note. One of these parameters was a low level of hemoglobin. Based on laboratory test references, a significant increase and a meaningful decrease have been observed in the hemoglobin level impact on HF symptoms and mortality. [13]

Another parameter was natriuretic peptides (BNP and pro-BNP), a marker in the diagnosis and prognosis of myocardial disease. This marker is released from the heart; it is checked as a test to evaluate the function of the cardiovascular and renal systems. [15] An increase in the BNP level is correlated with the severity of heart disease and its prognosis. [13]

In summary, our study showed that some simple parameters had an impact on WRF and adverse in-hospital outcomes in patients with AHF and can, thus, assist in the optimal management of this group of patients. Given the cost-effectiveness and availability of these parameters, they can be applied in acute settings in the emergency department.

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