Echocardiographic predictors of worsening renal function in acute heart failure: observations from the RASHF registry

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Abstract

Aims Echocardiography is known as the most useful diagnostic test in the assessment of patients with heart failure (HF), and the prognostic significance of echocardiographic findings in HF is well known. In this report, we aim to present the prognostic significance of a limited set of echocardiographic parameters obtained within 24 h of admission of patients enrolled in the Rajaie Acute Systolic Heart Failure registry.

Methods and results A total of 230 patients with the diagnosis of acute systolic HF (left ventricular ejection fraction ≤ 35%) were enrolled into the study. Transthoracic echocardiography was performed for all study population within 24 h of admission. The primary endpoint of the study was the occurrence of worsening renal function (WRF) during the hospitalization course. Acquiring data of transthoracic echocardiography within 24 h of admission was feasible in all study participants. The median (inter-quartile range) of left ventricular ejection fraction was 20% (15–23%). Severe right ventricular dysfunction was observed in 21.5% of patients. The grade of inferior vena cava collapse and right ventricular systolic dysfunction were associated with WRF. In multivariable analysis, right ventricular systolic dysfunction was among the independent predictors of WRF ($\beta = 0.8$, $P = 0.01$, odds ratio (OR) = 2.4 (1.2–4.9)) and in-hospital mortality ($\beta = 0.6$, $P = 0.04$, OR = 1.5 (0.5–4.6)).

Conclusions Echocardiographic parameters are useful for baseline assessment and provide additional information besides other clinical variables for prognostication. Right ventricular dysfunction is the most important risk factor in developing WRF and in-hospital mortality in patients with acute HF.

Keywords Acute heart failure; Echocardiography

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Introduction

Echocardiography is recommended as a useful diagnostic tool in the clinical setting of acute heart failure (AHF) by current HF guidelines. However, despite guideline recommendations, the timing of echocardiographic assessment and prognostic significance of echocardiographic findings in the setting of AHF have not been adequately described. In a recent study in the USA, two out of five patients did not undergo assessment of left ventricular ejection fraction (LVEF) after a new diagnosis of AHF. In another study in Europe, 68% of the 9400 patients admitted with AHF did not have an echocardiogram performed at some point during the index admission.

The Rajaie Acute Systolic Heart Failure (RASHF) registry is a single-centre, prospective, observational, hospital-based study of systolic HF patients admitted with AHF in a tertiary centre for advanced HF and transplantation programmes in Tehran, Iran. The main goals of this study were to clarify patients’ characteristics and their outcome in our region, comparing findings with those of other studies and identifying the
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prognostic factors. In this report, we aim to present the prog-
nostic significance of a limited set of echocardiographic pa-
rameters obtained within 24 h of admission of patients
enrolled in the RASHF registry.

Methods

In the RASHF registry, all AHF patients with an LVEF ≤ 35% were enrolled consecutively for 10 months from March 2012 to February 2013.

The study protocol and inclusion criteria have been described previously.4 All the study participants were subsequently followed up for 3 months for death or re-
hospitalization. The primary endpoint of the study was the occurrence of worsening renal function (WRF) during the hospitalization course. The secondary endpoints were in-
hospital mortality and death within 3 months after discharge.

WRF was defined as an absolute increase in serum Cr ≥ 0.3 mg/dL from baseline in at least two consecutive sam-

dles during the index hospitalization up to discharge.4–8

This study was approved by research and ethics committee

of Rajaie Cardiovascular Medical and Research Center, and written informed consent was obtained from all study participants.

The echocardiography protocol

Transthoracic echocardiography using a commercial GE Vivid 3 with a 3-MS variable frequency harmonic phased-array

transducer was performed by expert cardiologists for all study population within 24 h of admission in accordance with the American Society of Echocardiography guidelines.9–11

In order to perform a centralized echocardiographic evalu-
ation, the initial echocardiogram was obtained considering a

list of definitions for various echocardiographic parameters

(Table 1).

For all patients, a comprehensive transthoracic echocardi-
diography was performed during the hospital course before discharge. However, in this study, the first echocardiographic

findings acquired within first 24 h of admission were consid-
ered in statistical analysis.

All data were registered in software designed by dedi-
cated hospital information technology team (Supporting

Information).

The appropriate echocardiographic parameters including

left ventricular (LV) systolic and diastolic function, right ven-

tricular (RV) size and systolic function, presence of left atrial

enlargement, any valvular dysfunction and pulmonary artery

systolic pressure (PASP), and the size and collapse of inferior

vena cava (IVC) were taken into consideration. Owing to critical

condition of patients, the LV systolic function was assessed in terms of the ejection fraction (LVEF) by visual as-
essment; however, the biplane Simpson method was applied

in some more stable patients. LV diastolic dysfunction was

assessed and estimated by early and late mitral inflow

(E and A) as well as septal early diastolic (E’) velocities (E/A ratio and E/E’ ratio) and left atrial size.12,13 RV systolic

function was evaluated using the following parameters: tissue

Doppler-derived tricuspid lateral annular systolic velocity

(S’) and tricuspid annular plane systolic excursion (TAPSE) S’

Table 1 A list of definitions for various echocardiographic parameters

| Echocardiographic data                          | Comment                                      |
|-----------------------------------------------|----------------------------------------------|
| LVEF                                          | Visual estimation or by plane Simpson method |
| More-than-moderate LV enlargement             | ≥35 mm/m²                                    |
| Severe RV enlargement                         | Basal RV dimension ≥ 39 mm                   |
| Severe LV diastolic dysfunction in sinus rhythm| E/A velocity ratio ≥ 2                       |
| Significant RV dysfunction                     | Average E/e’ > 15                            |
| More-than-moderate MR                         | Basal RV S’ velocity < 10 cm/s               |
| More-than-moderate TR                         | TAPSE < 16 mm                                |
| More-than-moderate AR                         | Jet area/LA area ≥ 20%                       |
| More-than-moderate MS                         | Colour flow jet area ≥ 4 cm²                 |
| More-than-moderate AS                         | Jet area in central jets > 5 cm²             |
| Items to be measured                          | Jet area/RA area ≥ 20%                       |
|                                              | PISA radius > 0.6 cm                         |
|                                              | Dense jet density in CW Doppler              |
|                                              | Central jet height/LVOT diameter ≥ 50%       |
|                                              | Pressure half-time < 500 ms                  |
|                                              | MVA < 1.5 cm²                                |
|                                              | Aortic jet velocity > 3 m/s                  |
|                                              | Aortic mean gradient > 20 mmHg              |
|                                              | TAPSE, RV S’, IVC size and collapse, TRG, PSAP, LA area |

AR, aortic regurgitation; AS, aortic stenosis; CW, continuous wave Doppler; E, early mitral inflow velocity; E’, mitral annulus tissue velocity; IVC, inferior vena cava; LA, left atrial; LV, left ventricle; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; MR, mitral regurgitation; MS, mitral stenosis; MVA, mitral valve area; PASP, pulmonary artery systolic pressure; PISA, proximal isovelocity surface area; RA, right atrial; RV, right ventricle; S’, systolic tissue velocity; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; TRG, tricuspid regurgitation gradient.

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velocity < 10 cm/s and TAPSE < 16 mm indicated significant RV systolic dysfunction.\textsuperscript{13} The RV–pulmonary circulation coupling as a surrogate for the RV length–force relationship and a prognostic factor in HF was also calculated by a ratio of TAPSE/PASP.\textsuperscript{14}

### Statistical analysis

IBM SPSS Statistics 19 for Windows (IBM Corp, Armonk, NY, USA) was applied for all statistical analyses. One-sample Kolmogorov–Smirnov test was used to assess the normal distribution of variables. Categorical variables were presented as numbers (percentages), and quantitative variables were expressed as mean [standard deviation (SD)] or median [inter-quartile range (IQR)] as appropriate. Student’s \(t\)-test or Mann–Whitney \(U\)-test and \(\chi^2\) test or Kruskal–Wallis tests were used for comparisons and associations as appropriate. Binary multivariable regression analysis with stepwise selection method was used to define the independent predictors. \(P\) value < 0.05 was considered to be statistically significant.

### Results

Among >5000 admissions during 10 months, a total of 230 patients (82% male) with a mean (SD) age of 53 (16) were included in this study. Most of the patients have acute decompensated HF, and only 12% of them were diagnosed as acute de novo HF.

The demographic clinical and laboratory findings of study population were reported elsewhere.\textsuperscript{5} Table 2 depicts some of the study findings.

### Echocardiographic findings

In our centre, all newly admitted patients including patients suspected with AHF underwent transthoracic echocardiography on admission. Acquiring data of transthoracic echocardiography within 24 h of admission was feasible in all study participants, and almost all echocardiograms were acquired within the first 6 h of admission.

Table 3 shows the echocardiographic findings of study population.

The median (IQR) of LVEF was 20% (15–23%), and >60% of patients had moderate and/or moderate to severe LV enlargement. Fifty-six per cent of patients showed severe LV diastolic dysfunction, significant RV dysfunction was observed in 21.5% of patients, and 18.7% of patients had severe mitral regurgitation (MR).

### Table 2 Demographic and characteristics of all patients with acute heart failure, \(n = 230\)

| Characteristic                                      | Total \(n = 230\) |
|-----------------------------------------------------|------------------|
| Age, years, mean (SD)                               | 52 ± 16          |
| Gender, number (%)                                  |                  |
| Female                                              | 42 (18)          |
| Male                                                | 188 (82)         |
| Aetiology, number (%)                               |                  |
| Ischaemic cardiomyopathy                            | 128 (55.7)       |
| Non-ischaemic cardiomyopathy                        | 102 (44.3)       |
| Diabetes, number (%)                                | 77 (34)          |
| Hypertension, number (%)                            | 55 (24)          |
| Smoking, number (%)                                 | 75 (33)          |
| Previous MI, number (%)                             | 52 (23)          |
| Severe peripheral oedema, number (%)                | 128 (55)         |
| Ascites, number (%)                                 | 59 (26)          |
| Systolic BP, mm/Hg (mean, SD)                       | 110 ± 20         |
| Heart rate, b.p.m. (mean, SD)                       | 87 ± 20          |
| Atrial fibrillation rhythm, number (%)              | 48 (21)          |
| WRF, number (%)                                     | 67 (29.1)        |
| Daily dose (mg) of IV furosemide during admission, (mean, SD) | 158 ± 55         |
| Inotrope use during admission, number (%)           | 51 (22.1)        |
| Length of hospital stay, days (median, IQR)         | 9.5 (6–15)       |
| In-hospital death, number (%)                       | 22 (9.6)         |
| Death during 3 months after discharge, number (%)   | 34 (16.4)        |

BP, blood pressure; IV, intravenous; MI, myocardial infarction; SD, standard deviation; WRF, worsening renal function.

### Table 3 Echocardiographic data of patients with acute heart failure, \(n = 230\)

| Echocardiographic data                      | Value              |
|--------------------------------------------|--------------------|
| LVEF, %, median (IQR)                      | 20 (15–23)         |
| More-than-moderate                         | 145 (63)           |
| LV enlargement, number (%)                 | 53 (23)            |
| More-than-moderate LV enlargement, number  | 136 (59.1)         |
| Severe RV enlargement, number (%)          | 125 (54.3)         |
| More-than-moderate RV dysfunction, number  | 132 (57.5)         |
| More-than-moderate MR, number (%)          | 104 (45.1)         |
| More-than-moderate TR, number (%)          | 35 (15.2)          |
| More-than-moderate AI, number (%)          | 4 (1.8)            |
| More-than-moderate AS, number (%)          | 4 (1.8)            |
| TRG, mmHg, mean (SD)                       | 46.7 (14)          |
| Estimated PASP, mmHg, mean (SD)            | 53.2 (25.1)        |
| TAPSE, mm, mean (SD)                       | 15.1 (3.6)         |
| RV S\(^{-}\), cm/s mean (SD)               | 9.3 (2.6)          |
| IVC size, cm, median (IQR)                 | 1.9 (1.7–2.2)      |
| <50% IVC collapse, number (%)              | 117 (51)           |
| Left atrial area, cm\(^2\), mean (SD)      | 30 (8)             |
| RV–pulmonary artery coupling, mm/mmHg, median (IQR) | 0.29 (0.21–0.41) |

AI, aortic insufficiency; AS, aortic stenosis; IQR, inter-quartile range; IVC, inferior vena cava; LV, left ventricle; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MS, mitral stenosis; PASP, pulmonary artery systolic pressure; RV, right ventricle; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; TRG, tricuspid regurgitation gradient.
Prognostic significance of echocardiographic findings

Patients who developed WRF had significantly higher IVC size and lower IVC collapse. The median (IQR) of IVC size in patients with WRF was 2.1 (2.1–2.3) cm, whereas it was 1.75 (1.7–2.1) cm in patients without WRF (P = 0.03). All patients with WRF had an IVC size > 2.1 cm, and the IVC collapse was <50% in 66% of them (P = 0.002).

There was also a significant association between RV systolic dysfunction and development of WRF (P = 0.02). Seventy-three per cent of patients with WRF showed significant RV dysfunction (considering TAPSE < 16 mm and RV S’ velocity < 10 cm/s), whereas only 45% of patients without WRF had significant RV dysfunction. The median (IQR) of TAPSE in patients with and without WRF was 12 (11–14) mm and 16 (13–22) mm, respectively (P < 0.001). There was also significant difference between patients with and without WRF in terms of RV S’. The median (IQR) of RV S’ in patients with and without WRF was 8 (6–9) cm/s and 10 (8–14) cm/s, respectively (P < 0.001). There was no significant association between the severity of tricuspid regurgitation (TR), LVEF severity of LV diastolic dysfunction, and severity of MR or left atrial enlargement and development of WRF (all P values > 0.05).

The RV–pulmonary circulation coupling was significantly lower in patients with WRF. The median (IQR) of RV–pulmonary circulation coupling in patients with and without WRF was 0.25 (0.18–0.33) and 0.37 (0.27–0.63), respectively (P < 0.001). However, we found no independent correlation between RV–pulmonary circulation coupling and WRF in multivariable analyses.

The RV systolic dysfunction, baseline creatinine level > 1.5 mg/dL, and the presence of ascites were independent predictors of WRF in multivariable analyses (Table 4).

Regarding the relationship between echocardiographic data and in-hospital mortality, we found that significant RV dysfunction (P = 0.04), more-than-moderate TR (P = 0.02), severe LV diastolic dysfunction (P = 0.04), and RV–pulmonary circulation coupling were associated with higher in-hospital mortality. There was no association between in-hospital mortality and LVEF, severity of MR, or left atrial enlargement.

The severe RV systolic dysfunction, development of WRF, lower systolic blood pressure on admission, and presence of ascites were independent predictors of in-hospital deaths in multivariable analysis (Table 5).

However, the C statistic measures showed that by adding the significant RV dysfunction to the other clinical and laboratory factors in our multivariable models, the accuracy of model for prediction of only WRF and not in-hospital mortality was improved (Table 6).

Finally, the only variable associated with death within 3 months after discharge was severity of LV diastolic dysfunction, and none of the baseline echocardiographic findings were associated with mortality within 3 months after discharge in multivariable analyses.

Discussion

Our study results show that, besides the role of echocardiography in diagnosis of HF in patients who presented with dyspnoea or other relevant symptoms, echocardiographic parameters have prognostic significance and could be considered for risk stratification of patients with AHF. The uniform nature of our study population (AHF patients with LVEF < 35%), performing echocardiography within 6 h of admission and considering WRF as a prognostic factor are the strengths of our study.

There is no consensus recommendation regarding the optimal timing and re-assessment with echocardiography in AHF patients. In a review, Papadimitriou et al. have mentioned that as a result of variability in phenotypes of patients with AHF and lack of echocardiographic examination in many studies and trials, the usefulness of echocardiography for risk

Table 4 Predictors of worsening renal function (n = 230)

| Variable                                | Univariate model | Multivariate model* |
|-----------------------------------------|------------------|---------------------|
|                                         | β                | Wald               | P value | OR (95% CI) | β                | Wald               | P value | OR (95% CI) |
| Age                                     | 0.020            | 4.955              | 0.02    | 1.021 (1.002–1.04) | 0.8              | 4.786              | 0.02    | 2.4 (1.1–5.2)  |
| AF rhythm                               | 1.030            | 3.905              | 0.04    | 2.802 (1.008–7.8) | 0.9              | 4.42               | 0.03    | 2.5 (1.06–6.1)  |
| Ascites                                 | 1.012            | 11.99              | 0.001   | 3.01 (1.6–5.6) | 0.9              | 4.42               | 0.03    | 2.5 (1.06–6.1)  |
| Severe peripheral oedema                | 0.214            | 4.28               | 0.03    | 1.24 (1.01–1.5) | 0.9              | 4.42               | 0.03    | 2.5 (1.06–6.1)  |
| Baseline creatinine level > 1.5 mg/dL   | 0.796            | 11.23              | 0.001   | 2.21 (1.39–3.5) | 0.8              | 4.786              | 0.02    | 2.4 (1.1–5.2)  |
| IVC size                                | 0.153            | 2.35               | 0.03    | 1.1 (0.9–1.4) | 0.9              | 4.42               | 0.03    | 2.5 (1.06–6.1)  |
| Significant RV dysfunction              | 0.26             | 4.9                | 0.02    | 1.3 (1.03–1.6) | 0.8              | 6.07               | 0.01    | 2.4 (1.2–4.9)  |
| More-than-moderate TR                   | 0.09             | 0.08               | 0.7     | 0.9 (0.5–1.7) | 0.9              | 4.42               | 0.03    | 2.5 (1.06–6.1)  |
| Severe diastolic dysfunction            | 0.382            | 2.809              | 0.094   | 1.465 (0.937–2.290) | 0.9              | 4.42               | 0.03    | 2.5 (1.06–6.1)  |
| More-than-moderate MR                   | 0.063            | 0.02               | 0.9     | 0.960 (0.525–1.76) | 0.9              | 4.42               | 0.03    | 2.5 (1.06–6.1)  |
| Left atrial enlargement                 | 0.041            | 0.004              | 0.952   | 1.065 (0.560–2.028) | 0.9              | 4.42               | 0.03    | 2.5 (1.06–6.1)  |
| RV-pulmonary circulation coupling       | 3.7              | 16.1               | <0.001  | 0.02 (0.004–0.14) | 0.9              | 4.42               | 0.03    | 2.5 (1.06–6.1)  |

AF, atrial fibrillation; IVC, inferior vena cava; MR, mitral regurgitation; OR, odds ratio; RV, right ventricle; TR, tricuspid regurgitation.

*C statistic for this model is 0.71.
stratification in AHF is unclear. For example, in a European HF cohort, echocardiography was not performed in 68% of patients with AHF by the time of discharge, and less than half of patients who had an echocardiogram performed during the index admission were imaged within the first 24 h. In this HF cohort, about one-half of patients who had an earlier echocardiogram underwent a new one during the index admission. Although in some of the studies a comprehensive echocardiographic study has been performed in the setting of AHF, in many AHF studies and registries, only a few echocardiographic parameters such as LVEF, LV size variables, and LV diastolic parameters have been considered as variables.

Echocardiographic predictors of worsening renal function

One of the most important outcome measures in patients with AHF is WRF. Table 7 depicts some of the similar studies’ results regarding the prevalence and impact of WRF in patients with AHF. As shown in this table, most of these studies have emphasized on clinical and laboratory parameters as the predictors of WRF, and the significance of echocardiographic parameters in this regard is less studied. For example, in the POSH (Prospective Outcomes Study in Heart Failure) study, Cowie et al. assessed the prevalence and clinical predictors of 299 patients with AHF. The results of this study are very similar to what we found in the RASHF registry, but the echocardiographic parameters have not been considered in the POSH study. In another study by Metra et al., the prognostic significance of WRF was evaluated in 599 patients with AHF, and the only echocardiographic variable in this study was LVEF. In some other smaller studies like the Haglund et al. study, the diameter of RV in echocardiography was one of the independent predictors of WRF in AHF patients undergoing ultrafiltration, or in the Tandon et al. study, RV fractional area change and TAPSE were powerful predictors of WRF in patients with acute inferior wall myocardial infarction.

In the present study, we could show significant correlation between echocardiographic parameters and development of WRF during admission with AHF. The clinical predictors of WRF in our study have been presented previously. Among echocardiographic parameters, RV dysfunction was the most important predictor of WRF. We also found that the IVC size

| Table 5 | Predictors of in-hospital mortality |
|---------|------------------------------------|
| Variable | Univariate model | Multivariate model* |
|         | β        | Wald   | P value | HR (95% CI) | β        | Wald   | P value | HR (95% CI) |
| SBP     | 0.031    | 6.341  | 0.01    | 0.969 (0.946–0.993) | 0.04     | 6.4    | 0.01    | 0.9 (0.9–1.1) |
| Ascites | 1.6      | 12.8   | <0.0001 | 4.9 (2.05–11.9)   | 2.9      | 20     | <0.0001 | 19.1 (5.2–69.7) |
| WRF     | 1.8      | 15.2   | <0.0001 | 6.07 (2.4–15.03)  | 0.6      | 3.6    | 0.04    | 1.5 (0.5–4.6)  |
| LVEF    | 0.01     | 0.11   | 0.7     | 0.9 (0.9–1)       |          |        |         |             |
| IVC size| 0.05     | 0.12   | 0.7     | 0.9 (0.6–1.3)     |          |        |         |             |
| Significant RV dysfunction | 0.3 | 3.24  | 0.04    | 1.3 (0.97–1.8)    |          |        |         |             |
| More-than-moderate TR | 0.6 | 4.6   | 0.03    | 1.8 (1.05–3.16)   |          |        |         |             |
| Severe diastolic dysfunction | 0.5 | 1.9   | 0.04    | 1.6 (0.8–3.1)     |          |        |         |             |
| More-than-moderate MR | 0.3 | 0.64  | 0.4     | 1.4 (0.6–3.5)     |          |        |         |             |
| Left atrial enlargement | 0.8 | 0.475 | 0.5     | 2.1 (0.24–19)     |          |        |         |             |
| RV–pulmonary circulation coupling | 2.6 | 6.1   | 0.04    | 0.07 (0.006–0.89) |          |        |         |             |

HR, hazard ratio; IVC, inferior vena cava; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; RV, right ventricle; SBP, systolic blood pressure; TR, tricuspid regurgitation; WRF, worsening renal function.
*C statistic for this model is 0.87.

| Table 6 | C statistics measure for comparing the model using clinical and laboratory factors and the new model by adding significant right ventricular dysfunction |
|---------|----------------------------------------------------------------------------------|
| Model/predictor | C statistics (95% CI) |
| Outcome: worsening renal failure |                             |
| Model 1 | 0.63 (0.54–0.72) |
| Model 2 | 0.71 (0.63–0.79) |
| Outcome: mortality |                             |
| Model 1 | 0.86 (0.78–0.94) |
| Model 2 | 0.87 (0.81–0.93) |

RV, right ventricular.
Table 7 Comparison of the predictors of worsening renal function in the present study and previous investigations

| First author of study and year of publication | Design study, population | Number of patients | Predictor of WRF in univariate analysis | Predictor of WRF in multivariate analysis |
|-----------------------------------------------|--------------------------|-------------------|---------------------------------------|----------------------------------------|
| Verdiani,8 2011                               | Cohort, AHF              | 394               | Prior renal failure                   | Age > 75 years                         |
|                                               |                          |                   | Creatinine > 1.5 mg/dL                | Digoxin                                |
|                                               |                          |                   | Heart rate ≥ 100 b.p.m.               | Prior renal failure                    |
|                                               |                          |                   | Heart rate ≥ 100 b.p.m.               | Obesity                                |
|                                               |                          |                   | Increase in creatinine > 0.3 mg/dL    | Occurrence of hypotension < 90 mmHg    |
|                                               |                          |                   | Occurrence of hypotension < 90 mmHg   | within 12 h                            |
|                                               |                          |                   | Aldosterone antagonist treatment      | Increase in creatinine > 0.3 mg/dL     |
|                                               |                          |                   | LV geometry                           |                                        |
|                                               |                          |                   | Heart rate ≤ 65 b.p.m.                |                                        |
|                                               |                          |                   | RV/LV diastolic dimension (mL)        |                                        |
|                                               |                          |                   | PASP (mmHg)                           |                                        |
| Kawase,7 2016                                 | Retrospective cohort, AHF| 205               | Increase in creatinine ≥ 0.3 mg/dL    | Occurrence of hypotension < 90 mmHg    |
|                                               |                          |                   | Occurrence of hypotension < 90 mmHg   | within 12 h                            |
|                                               |                          |                   | Age                                    |                                        |
|                                               |                          |                   | Diastolic blood pressure < 90 mmHg   |                                        |
|                                               |                          |                   | Aldosterone antagonist treatment      | E/E > 15                               |
|                                               |                          |                   | LV geometry                           |                                        |
|                                               |                          |                   | Heart rate ≤ 65 b.p.m.                |                                        |
|                                               |                          |                   | RV/LV diastolic dimension (mL)        |                                        |
|                                               |                          |                   | PASP (mmHg)                           |                                        |
| Raichlin,5 2014                               | Cohort, AHF              | 99                | Aldosterone antagonist treatment      | History of renal failure               |
|                                               |                          |                   | LV geometry                           | Spironolactone during                  |
|                                               |                          |                   | Heart rate ≤ 65 b.p.m.                | first 6 months                         |
|                                               |                          |                   | RV/LV diastolic dimension (mL)        | Maximal increase in                    |
|                                               |                          |                   | PASP (mmHg)                           | loop diuretic dose                      |
|                                               |                          |                   |                                        |                                        |
| Belziti,27 2009                               | Retrospective cohort, AHF| 200               | Age                                    | Hypertension                           |
|                                               |                          |                   | Ischaemic aetiology                   | Diabetes                               |
|                                               |                          |                   | Serum creatinine, GFR, SBP            | Age                                    |
|                                               |                          |                   | History of treatment with ACE-I/ARBs  | Diuretic use                            |
|                                               |                          |                   | and antialdosterone agents            |                                        |
|                                               |                          |                   | Intravenous furosemide during         |                                        |
|                                               |                          |                   | admission                              |                                        |
|                                               |                          |                   |                                        |                                        |
| Maeder,21 2012                                | Sub-study RCT, AHF       | 566               | Renal failure                         | Hypertension                           |
|                                               |                          |                   | NT-pro-BNP                            | Diabetes                               |
|                                               |                          |                   | BUN                                   | Age                                    |
|                                               |                          |                   | Haemoglobin                           | Diuretic use                            |
|                                               |                          |                   | Orthopnoea                            |                                        |
|                                               |                          |                   | Oedema                                |                                        |
|                                               |                          |                   | Hepatomegaly                           |                                        |
|                                               |                          |                   | Loop diuretic                         |                                        |
|                                               |                          |                   | Loop diuretic dose                    |                                        |
|                                               |                          |                   |                                        |                                        |
| Damman,28 2014                                | Meta-analysis, AHF       | 49,890            | Baseline GFR                          | Hypertension                           |
|                                               |                          |                   | Hypertension                          | Diabetes                               |
|                                               |                          |                   | Diabetes                              | Age                                    |
|                                               |                          |                   | Diuretic use                           | Diuretic use                            |
|                                               |                          |                   |                                        |                                        |
| Sani,29 2014                                 | Registry, AHF            | 1006              | Rales                                 | Rales                                 |
|                                               |                          |                   | Peripheral oedema                     | Body mass index                        |
|                                               |                          |                   | Body mass index                       |                                        |
| Cowie,17 2006                                 | Cohort, AHF              | 299               | Serum creatinine on admission         | Atrial fibrillation                    |
|                                               |                          |                   | Atrial fibrillation                   | Pulmonary oedema                       |
|                                               |                          |                   | Insulin-treated diabetes              |                                        |
|                                               |                          |                   | Serum creatinine                      |                                        |
|                                               |                          |                   | Pulmonary oedema                      |                                        |
| Tandon,18 2013                                | Cohort (acute RVMI)      | 48                | History of diabetes mellitus          | History of diabetes mellitus           |
|                                               |                          |                   | Cardiogenic shock at presentation     | Cardiogenic shock at presentation      |
|                                               |                          |                   | TAPSE                                 | TAPSE                                  |
|                                               |                          |                   | RVFAC                                 | RVFAC                                  |
|                                               |                          |                   | Raised serum aminotransferase and     | Raised serum aminotransferase and      |
|                                               |                          |                   | INR                                   | INR                                    |
|                                               |                          |                   |                                        |                                        |
| Soltani, present study                        | Registry                | 230               | Age                                    | Ascites                                |
|                                               |                          |                   | AF rhythm                             | Baseline creatinine level > 1.5 mg/dL  |

(Continues)
and collapse (two good indices for right heart function) were correlated with WRF. All of these findings are consistent with the results of numerous studies that show that right heart function is more important than LVEF in the development of cardiorenal syndrome.19–22 However, the presence of significant RV dysfunction and increased IVC size shows more progressive HF and poor outcome in these patients.

It has been recently shown that the ratio of TAPSE/PASP (RV–pulmonary circulation coupling) has prognostic significance in patients with HF irrespective of preserved or reduced LVEF.14 In our study, we could find a correlation between RV–pulmonary circulation coupling and both WRF and in-hospital mortality in univariable analysis, and the RV–pulmonary circulation coupling was significantly lower in patients with WRF and/or those who died in hospital. However, as shown by multivariable analyses, this ratio could not independently predict WRF or in-hospital death in the setting of AHF. For as far as we have studied and researched, there is no published study that investigates the RV–pulmonary circulation coupling in the setting of AHF, and determination of its prognostic significance in the setting of AHF would be a new line for investigation.

Echocardiographic predictors of in-hospital mortality

There are conflicting data regarding the echocardiographic predictors of in-hospital mortality in AHF; some studies showed LVEF and TR gradient as important predictors of early death during admission,12,16,23 and some other studies could not show any association between LVEF and major adverse events including in-hospital mortality.24 Citro et al. determined echocardiographic and clinical correlates of AHF, cardiogenic shock, and in-hospital death in a cohort of takotsubo cardiomyopathy. They performed a comprehensive echocardiographic examination within 6 h of admission in these patients feasibly and showed the higher age, lower LVEF, higher E/E’ ratio, and more severe MR as independent predictors of major adverse events.25

We could not also find any association between LVEF and in-hospital death, which may be a result of the nature of our study population. Many enrolled patients had advanced HF with very severe LV systolic dysfunction and poor prognosis; therefore, LVEF might not be a predictor for in-hospital mortality in our study.

The severity of LV diastolic dysfunction has been shown as another important and powerful predictor of short-term and long-term mortality of patients with AHF.10,12,26

In the present study, although severe LV diastolic dysfunction was significantly correlated with in-hospital mortality in univariable analysis, we found no association in multivariable analysis, which might be explained by the critical clinical condition of our study population.

Another echocardiographic correlate of early and late HF mortality and re-admission in AHF patients with reduced ejection fraction is RV function (evaluated by the TAPSE, tricuspid annular velocities, or RV peak systolic strain).12,18,23 In this regard, we similarly found the significant RV dysfunction as an independent predictor of in-hospital mortality.

Study limitations

The most important limitation of this study is its nature of being registry, and like any observational study, the possibility for introducing bias through unmeasured confounding variables exists.

Although a list of definitions for various echocardiographic parameters was provided, the interpretation of echocardiographic study might be at the discretion of the person performing the study. In the present study, measuring natriuretic peptides was not possible for all patients. Finally, the follow-up duration is only 3 months. The Iranian HF registry is ongoing, and we will try to overcome the limitations in future studies.

In conclusion, the presence of RV dysfunction in echocardiography is the most important risk factor in developing WRF and in-hospital mortality in AHF. Performing

| First author of study and year of publication | Design study, population | Number of patients | Predictor of WRF in univariable analysis | Predictor of WRF in multivariate analysis |
|---------------------------------------------|--------------------------|-------------------|----------------------------------------|------------------------------------------|
| ACE-I, angiotensin-converting enzyme inhibitor; AHF, acute heart failure; ARB, angiotensin receptor blocker; BUN, blood urea nitrogen; GFR, glomerular filtration rate; IHD, ischaemic heart disease; INR, international normalized ratio; LV, left ventricle; LVEF, left ventricular ejection fraction; NT-pro-BNP, N-terminal pro-BNP; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; RCT, randomized controlled trial; RV, right ventricular; RVFAC, RV fractional area change; RVMI, RV myocardial infarction; SBP, systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion; WRF, worsening renal function. | Ascites | Severe peripheral oedema | Baseline creatinine level > 1.5 mg/dL | Significant RV dysfunction |
Echocardiography in patients with AHF within 24 h of hospital admission is feasible. Echocardiographic parameters are useful for baseline assessment and provide additional information besides other clinical variables for prognostication.

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Conflict of interest

None declared.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1 Echocardiography form of Rajaie acute systolic heart failure registry software.

Figure S2 Some of the acquired echocardiographic parameters in early admission echocardiography.

Figure S3 Some of the acquired echocardiographic parameters in early admission echocardiography (continue).
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