

Original Paper

Clinical and Echocardiographic Predictors of Cardiorenal Syndrome Type I in Patients with Acute Ischemic Right Ventricular Dysfunction

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Key Words

Clinical predictors · Echocardiographic predictors · Cardiorenal syndrome · Acute ischemic right ventricular dysfunction

Abstract

Background: In current cardiology practice, the importance of acute cardiorenal syndrome (CRS) in determining the outcome of patients with acute coronary syndrome (ACS) is well recognized. Certain groups of ACS patients are at higher risk of developing CRS. Data on the association between right ventricular (RV) functions and CRS after acute myocardial infarction (AMI) are scarce. The purpose of the current study was to evaluate the relation between RV function and the development of CRS in patients presenting with inferior wall AMI and RV involvement. **Patients and Methods:** Patients with inferior wall AMI with RV involvement underwent echocardiography at admission to assess RV function. RV functions were quantified according to RV fractional area change (RVFAC), tricuspid annular plane systolic excursion (TAPSE), and RV outflow tract fractional shortening (RVOTFS). The patients were followed up until discharge from hospital. All patients who developed CRS were included in group I, all patients who did not develop CRS were included in group II (controls). Multivariate analysis was carried out to determine the significance of the echocardiographic and clinical parameters in predicting the development of CRS in these patients. **Results:** In our study, a history of diabetes mellitus, cardiogenic shock at admission, and RVFAC and TAPSE could significantly predict the development of CRS in patients presenting with inferior wall AMI and RV involvement. **Conclusions:** RV functions provide strong prognostic information regarding the development of CRS in patients of inferior wall AMI with RV involvement.

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Background

In current cardiology practice, the importance of acute cardiorenal syndrome (CRS) in determining the outcome of patients with acute coronary syndrome (ACS) is well recognized. Certain patients with ACS are at higher risk of developing CRS type I. Acute ischemic right ventricular (RV) systolic dysfunction is an appropriate milieu for the development of CRS, as it is accompanied by a decreased forward cardiac output and an increased renal venous back pressure, subsequently leading to a decrease in the net glomerular filtration rate and acute renal failure [1–3]. Data on the correlative association between RV functions and CRS after acute myocardial infarction (AMI) are scarce. The purpose of our study was to evaluate predictors for the development of CRS type I in patients with inferior wall AMI associated with ischemic RV dysfunction in relation to RV functions measured by echocardiography.

Patients and Methods

This was a prospective study based on the protocols of patients presenting in the emergency room of a tertiary care cardiac center over a period of 1 year. Out of 552 patients admitted for AMI in that year, 408 patients had anterior wall myocardial infarctions and 144 had inferior wall myocardial infarctions. 52 patients had concomitant RV myocardial infarction. All these patients underwent echocardiography at admission. Out of the 52 patients screened, 48 patients were enrolled as they had inferior wall AMI with RV involvement. Their RV functions were assessed taking the following parameters into account: RV fractional area change (RVFAC), tricuspid annular plane systolic excursion (TAPSE), and RV outflow tract fractional shortening (RVOTFS). The patients were followed up until discharge from the hospital.

Exclusion Criteria

Patients with chronic kidney disease, previous coronary artery disease with severe left ventricular systolic dysfunction, valvular heart disease, or chronic obstructive pulmonary disease were excluded.

Definitions and Clinical Features

The diagnosis of RV myocardial infarction was based on an ST segment elevation >1 mV in lead V4R with a concomitant ST segment elevation in inferior leads at admission and a right-side chamber dilatation with regional wall motion abnormality in the right coronary artery's territory segmental supply on echocardiography.

The diagnosis of CRS type I was based on the development of acute renal failure, i.e. a decrease in urine output <0.5 ml/kg/h along with a rise in creatinine of 0.3 mg/dl from baseline within 72 h of admission in patients with inferior wall AMI with RV involvement [4–9].

The following baseline clinical features were noted: a history of diabetes mellitus, smoking status, and hypertension. Additionally, the hospital course including modality of primary treatment, time to thrombolysis/revascularization, and coronary angiography findings, single-vessel or multi-vessel disease, and patient outcome were recorded.

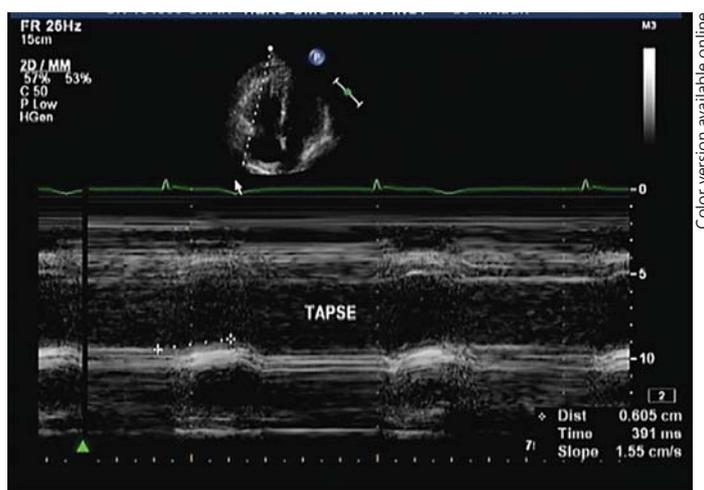
The patients were divided into 2 groups: all patients who developed CRS type I were included in group I; all patients who did not develop CRS type I were included in group II (control).

Echocardiography

Echocardiographic images were obtained with the patients in the left lateral decubitus/supine position using a commercially available system (hp SONOS 4500/Philips Envisor). Data acquisition was performed with a 3.5- to 5-MHz transducer at a depth of 14–18 cm in the parasternal and apical views. The patients were asked to hold their breath, while the M-mode and 2-dimensional images were taken. Five consecutive beats were saved in cine loop format. The reference limits of the echocardiographic measurements were defined according to American Society of Echocardiography (ASE) guidelines [10–16].

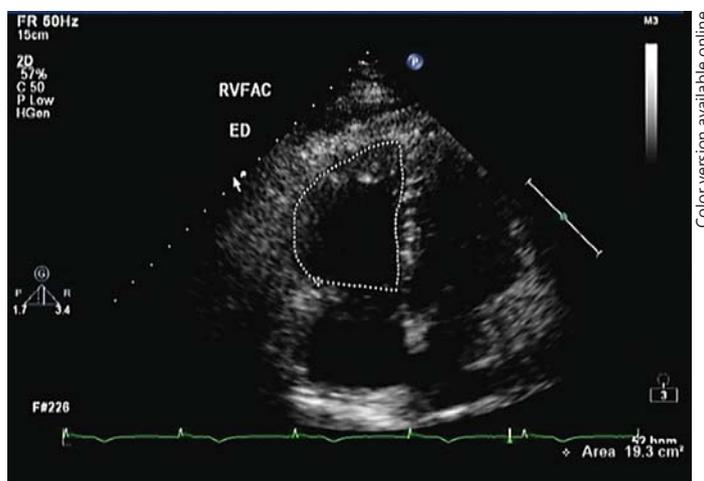
After the baseline echocardiographic examination – including left ventricular ejection fraction estimation – the following RV function parameters were taken: RVFAC was analyzed on the two-dimensional images by tracing the RV end-diastolic area (RVDA) and the RV end-systolic area (RVSA) in the apical

Fig. 1. TAPSE, an M-mode parameter, shows the systolic excursion of the tricuspid annulus from base to apex in systole [17].



Color version available online

Fig. 2. RVFAC, a 2-dimensional parameter, shows the fractional area change of the RV in a cardiac cycle [20].



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4-chamber view using the formula $(RVDA - RVSA)/RVDA \times 100$. TAPSE was measured in the apical 4-chamber view by placing the M-mode cursor through the tricuspid annulus in such a way that the annulus moved along the M-mode cursor. The total displacement of end-diastole to end-systole was calculated in millimeters. RVOTFS was measured above the aortic valve in the standard PSAX view. The data were recorded using the M-mode cursor at the proximal RV outflow tract (RVOT) level and analyzed using the formula: $RVOT_{end-diastole} - RVOT_{end-systole}/RVOT_{end-diastole} \times 100$. Normal ranges as per ASE guidelines were: 32–60% for RVFAC, 35–42% for RVOTFS, and 20 ± 3 mm for TAPSE [17–23]. Echocardiographic images and data were analyzed by 3 experienced and trained observers (fig. 1–4).

Statistical Analysis

Continuous data are presented as mean \pm standard deviation and categorical data are presented as frequencies and percentages. Statistical analysis was done using both univariate (ANOVA, z test) and multivariate (logistic regression) equations. The primary aim was to assess the association between echocardiographic parameters of RV functions and the development of CRS type I after adjusting for covariates. Separate multivariate models were constructed for RVFAC, TAPSE and RVOTFS. Cox proportional hazards analysis was used to evaluate the individual prognostic importance of the various parameters to avoid colinearity with other parameters. For RVFAC, RVOTFS, and TAPSE, the cutoffs were defined according to the ASE guidelines: 32%, 50%, and 1.5 cm, respectively [17, 20, 23]. Univariate and multivariate Cox proportional hazards analysis was performed, dichotomized by the cutoffs. All statistical tests were 2-sided, and a probability value <0.05 was considered statistically significant.

This study has been approved by the institute's Committee on Human Research.

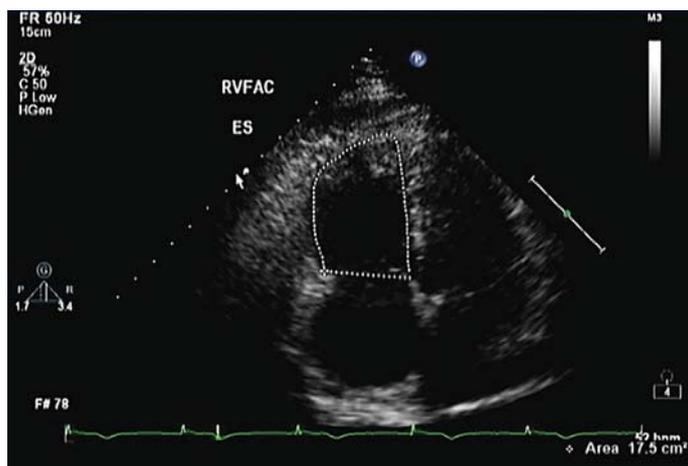


Fig. 3. RVFAC, a 2-dimensional parameter, shows the fractional area change of the RV in a cardiac cycle [20].

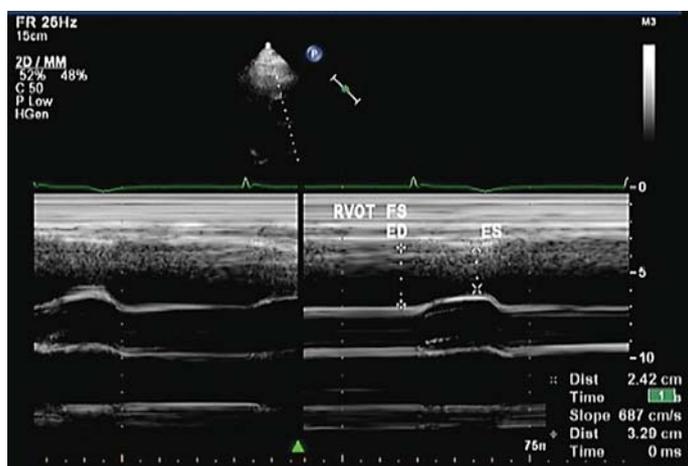


Fig. 4. RVOTFS, an M-mode parameter [23].

Results

Out of a total of 48 patients, 28 (58.34%) patients developed CRS type I, 25 (52%) patients presented with shock at admission, 15 (65.22%) of these 25 patients developed CRS. Amongst the demographic and echocardiographic parameters, a history of diabetes mellitus and cardiogenic shock at presentation were significantly associated with the development of CRS type I ($p = 0.042$ and 0.008 , respectively), while age, gender, a history of smoking, and hypertension were not ($p = 0.144$, 0.282 , 0.158 , and 0.676 , respectively). The echocardiographic parameters TAPSE and RVFAC were significantly reduced in group I ($p = 0.008$ and 0.042 , respectively), while RVOTFS was not ($p = 0.539$). The cutoff values for RVFAC and TAPSE for the development of CRS were 18.77% and 15.71 mm, respectively. Left ventricular ejection fraction was not significantly associated with the development of CRS ($p = 0.536$). Amongst the laboratory parameters, raised serum aminotransferase and INR values were significantly associated with the development of CRS ($p = 0.088$ and 0.039 , respectively).

Twenty patients received primary treatment [15 (31%) patients underwent thrombolysis and 5 (10%) patients primary percutaneous coronary intervention (PCI)]. Five (25%) patients in the thrombolysis group developed CRS, while none in the primary PCI group developed CRS. The remaining 28 patients were in the non-revascularized group, i.e. they did not receive either thrombolysis or primary PCI due to a delay in the presentation. Seventeen (60%) patients in this group developed CRS. Coronary angiography could only be done in 25

(52%) patients. Ten (40%) patients had single-vessel disease, 2 out of those developed CRS; 15 (60%) patients had multi-vessel disease, 3 out of those developed CRS. No significance could be ascertained due to the small number of patients.

Predictors of CRS Type I

After multivariate analysis, amongst the clinical parameters, a history of diabetes mellitus and shock at presentation were independently associated with the development of CRS type I ($p = 0.042$ and 0.008 , respectively), along with the laboratory parameters serum aminotransferase and INR.

TAPSE and RVFAC were also significant predictive parameters ($p = 0.008$ and 0.042 , respectively). Univariate analysis showed a sensitivity of 82 and 91% for TAPSE (cutoff value: 15.37 mm) and RVFAC (cutoff value: 18.77%), respectively. Though they were less in number, the revascularized patients had fewer incidences of CRS (25%) than the non-revascularized group (60%).

Discussion

CRS type I is an increasingly recognized entity in patients presenting in cardiac emergency units. There are few markers for its early diagnosis and they are not well-defined. Various clinical parameters and biomarkers have been studied in CRS patients with heart failure; however, few studies are available on AMI patients with CRS. RV AMI patients usually present with systemic venous congestion and hypoperfusion due to RV pump failure causing passive venous congestion. Increased renal venous pressure results in a cascade of events, which lead to the development of acute CRS [11–15]. Acute ischemic RV dysfunction therefore provides an apt setting to study CRS type I.

In the present study, we found the following clinico-laboratory and echocardiographic predictors of CRS type I: a history of diabetes mellitus, cardiogenic shock at presentation, raised INR and serum aminotransferase values (>1.5 and >500 IU, respectively), and reduced TAPSE and RVFAC values (cutoff value: 15.37 mm and 18.77%, respectively). Our findings also showed that those patients who developed CRS had a higher in-hospital mortality rate (35%).

The incidence of CRS type I occurring after ACS ranges between 11 and 19.5% [6–10]. This wide range may be responsible for the differences in the definitions used to determine worsening renal function and the differences in the subgroups of enrolled patients. We had a higher incidence of patients who developed CRS (58.34%) due to our patient selection, as only those with RV involvement were included, while other groups of ACS patients were excluded. Many studies have evaluated the association of various predictors with the occurrence of CRS especially in ACS patients, i.e. age, ejection fraction, diabetes, hypertension, and chronic kidney disease [6–9]. Most of these studies are secondary or post hoc analyses of large registry databases or clinical drug therapy trials, which included a large number of patients. We performed a small but prospective study to demonstrate that RV dysfunction is an important causative mechanism for the development of CRS, and we identified patients at increased risk for in-hospital mortality (with a sensitivity of 82.61% for TAPSE and 91.30% for RVFAC), while left ventricular ejection fraction was not significantly associated with CRS as expected. We also showed that patients who had received early revascularization (thrombolysis or primary PCI) had reduced incidences of acute CRS. Although increased age was an important predictor of in-hospital mortality in previous studies on inferior wall myocardial infarction and RV involvement, this was not seen in our study, probably because the mean age of the patients enrolled was 65 years [10–15].

Limitations

The first limitation of our study is that we did not include GFR estimation; however, in many studies the same definition for acute CRS has also been used for defining patients. The second limitation is the use of traditional M-mode and 2-dimensional parameters for analyzing RV functions. Dedicated 3-dimensional echocardiographic and tissue Doppler imaging techniques are not available for our emergency cases, but the M-mode parameters used in our study (TAPSE, RVFAC, and RVOTFS) have proven sensitivity in estimating global RV functions in various studies [16–23]. The third limitation is the paucity of angiographic data. The impact of multi-vessel disease could not be fully excluded, though our data did not suggest a significant difference in mortality.

Conclusion

We found that CRS occurs frequently in patients with a history of diabetes mellitus and shock at presentation. These patients also have an increased in-hospital mortality rate if they are not revascularized in time. Although there are multifactorial causative mechanisms for CRS, estimating RV functions is helpful in guiding patient management and improving our collaborative clinical approach.

Disclosure Statement

None of the authors have any conflicts of interest.

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