

**CLINICAL AND ECHOCARDIOGRAPHIC PREDICTORS OF
CARDIORENAL SYNDROME TYPE 1 IN ACUTE CORONARY
SYNDROME WITH HEART FAILURE: A PROSPECTIVE
OBSERVATIONAL STUDY**

**THE NAMES AND AFFILIATIONS OF THE AUTHORS
CHETAN KUMAR PATTARI¹, SUDHA KUMARY V², RAKESH K³, S G SHYAM
LAKSHMAN³**

- 1- Senor Resident, Government Medical College, Kottayam, Keralam.
2- Associate Professor Cardiology, Government Medical College, Kannur, Keralam.
3- Assistant Professor Cardiology, Government Medical College, Kannur, Keralam.**

**CORRESPONDING AUTHOR
RAKESH K
ASSISTANT PROFESSOR CARDIOLOGY,
GOVERNMENT MEDICAL COLLEGE,
KANNUR, KERALAM.
PIN:670503
MOBILE NUMBER: 8281414511
EMAIL: rakeshunnikrishnan1984@gmail.com**

ABSTRACT

BACKGROUND: Cardiorenal syndrome type 1 (CRS1) refers to the acute worsening of cardiac function leading to acute kidney injury (AKI) and is commonly seen after an acute coronary syndrome (ACS) or acute heart failure. It is associated with increased morbidity and mortality. Understanding the clinical features and hemodynamic factors that predict CRS1 in ACS patients is crucial in developing accurate risk prediction tools and facilitating early, targeted clinical management.

AIMS AND OBJECTIVES: To determine the incidence of Cardiorenal syndrome type 1 in patients presenting with acute coronary syndrome with heart failure and its association between clinical features and echocardiographic findings.

METHODS: A single-centre, prospective observational study. The study evaluated 70 patients admitted with ACS and heart failure. Patients with alternate causes of AKI, acute on chronic kidney disease (CKD), or prior nephrotoxic drug use were excluded. Baseline clinical characteristics, laboratory parameters and detailed echocardiographic parameters were recorded. Statistical methods, including binary logistic regression and ROC curve analysis, were employed to identify and quantify independent predictors of CRS1.

RESULTS: Of the 70 patients 98.6% presented with an ST-Elevation Myocardial Infarction (STEMI). CRS1 developed in 67.1% of the cohort. Multivariable logistic regression revealed that Right Ventricular Myocardial Infarction (RVMI) was the most powerful independent predictor (OR=27.77, p=0.005), followed by LVEF < 40% (OR=14.04, p=0.024). ROC curve analysis identified LVEF by Simpson's method as the most robust predictor (AUC=0.72). Diastolic markers—specifically Mitral E/e' ratio and E-deceleration time (EDT)—demonstrated high predictive accuracy (both AUC=0.69), outperforming right-sided metrics like RVTAM (AUC=0.58) and RV S' velocity (AUC=0.50). Other univariable predictors included raised JVP, diabetes mellitus, and anterior wall MI.

CONCLUSION: CRS1 affects a substantial majority of patients with ACS and heart failure. The findings validate a "dual-hit" pathophysiological paradigm where severe systemic venous congestion and critical arterial underfilling act as simultaneous catalysts for AKI. The high predictive value of LVEF and diastolic indices (E/e', EDT) highlights the urgent need for early echocardiographic risk stratification to identify vulnerable patients and initiate aggressive clinical management.

KEYWORDS: Acute Coronary Syndrome; Heart Failure; Cardiorenal syndrome-1; Right Ventricular Myocardial Infarction.

Introduction

The heart and kidneys share a complex physiological relationship, wherein dysfunction of one organ often precipitates dysfunction in the other. Cardiorenal syndrome (CRS) represents this bidirectional interaction and is associated with high morbidity and mortality [1, 2]. Cardiorenal syndrome type 1 (CRS1) is characterized by acute deterioration of cardiac function leading to acute kidney injury (AKI). It is commonly observed following acute coronary syndrome (ACS), acute heart failure, or cardiogenic shock [1, 3]. Despite advances in reperfusion strategies, CRS1 remains a major determinant of adverse outcomes [4, 5].

Traditionally, reduced cardiac output was considered the primary driver of renal dysfunction. However, emerging evidence highlights the role of venous congestion, elevated central venous pressure, and diastolic dysfunction as critical contributors [6, 7, and 8]. Echocardiography offers a non-invasive means to evaluate both systolic and diastolic function, making it an essential tool for early risk stratification [13, 14]. This study aims to identify

clinical and echocardiographic predictors of CRS1 in ACS patients with heart failure, thereby facilitating early diagnosis and targeted management.

METHODOLOGY

This study was designed as a single-center, prospective observational study conducted over a period of 12 months at a tertiary care cardiac center. A total of 70 consecutive patients admitted with acute coronary syndrome (ACS) complicated by heart failure were enrolled after obtaining informed consent and institutional ethics approval. ACS and heart failure were diagnosed based on clinical features and guideline-directed definitions [9, 10, and 11]. Patients aged >18 years were included, while those with pre-existing chronic kidney disease, acute-on-chronic kidney injury, prior heart failure, valvular heart disease, malignancy, or exposure to nephrotoxic drugs were excluded to minimize confounding factors influencing renal outcomes. The sample size was calculated based on prior studies reporting an incidence of CRS1 of approximately 58%, ensuring adequate statistical power for predictive modeling [4].

Baseline clinical data, including demographic characteristics, cardiovascular risk factors, hemodynamic parameters, and Killip classification, were recorded using a structured proforma. Laboratory investigations included serial measurements of serum creatinine, estimated glomerular filtration rate (eGFR), cardiac biomarkers, and urinary albumin. Cardiorenal syndrome type 1 (CRS1) was defined according to the KDIGO criteria, as an increase in serum creatinine ≥ 0.3 mg/dL within 48 hours or ≥ 1.5 times baseline [12]. Renal function was reassessed at 48 hours to capture early AKI, which has been shown to correlate strongly with adverse outcomes in ACS populations [5, 20].

Comprehensive transthoracic echocardiography was performed in all patients using standardized protocols recommended by the American Society of Echocardiography and the European Association of Cardiovascular Imaging [13]. Left ventricular ejection fraction (LVEF) was assessed using Simpson's biplane method, while diastolic function was evaluated using transmitral inflow velocities (E/A ratio), tissue Doppler imaging (e' velocity), and calculation of the E/ e' ratio as a surrogate for left ventricular filling pressures [14, 17, and 18]. Right ventricular function was assessed using tricuspid annular motion parameters. Statistical analysis was performed using Jamovi software, with continuous variables expressed as mean \pm SD and categorical variables as percentages. Associations were tested using chi-square and independent t-tests. Receiver operating characteristic (ROC) curve analysis was used to determine predictive accuracy, univariable and multivariable logistic regression identified independent predictors of CRS1. A p-value < 0.05 was considered statistically significant.

RESULTS

The study cohort consisted of 70 patients with a mean age of 60.3 ± 9.0 years, with a predominance of males (65.7%). The clinical presentation was overwhelmingly dominated by STEMI (98.6%), reflecting a population with high ischemic burden. The overall incidence of CRS1 was notably high at 67.1%, indicating a substantial burden of acute cardiorenal interaction in this high-risk cohort. Baseline comorbidities were prevalent, with hypertension (71.4%), dyslipidemia (60%), and diabetes mellitus (50%) being the most common. Despite a high rate of revascularization (94.3%), a significant proportion of patients developed CRS1, highlighting that reperfusion alone does not prevent cardiorenal deterioration. (Table1)

Table 1: Baseline characteristic

Total cases-70	Mean/Percentage
Age Mean	60.3± 9.0 years
Sex Ratio/percentage	Male: 46 (65.7%) Female: 24(34.3%)
BMI	Normal: 41 (58.6%) Overweight: (29 41.4%)
Diabetes Mellitus	35 (50%)
Hypertension	50 (71.4%)
Dyslipidemia	42 (60%)
Prior CAD	14 (20%)
Smoking	15 (21.4%)
Old CVA	7 (10%)
Pulse	In Sinus rhythm-62(88.6%) In Arrhythmia-8 (11.4%)
Blood pressure	SBP-126.5mmHg ± 28.4 DBP-77.2mmHg ± 14.7
JVP	Normal-50 (71.4%) Raised-20(28.6%)
NSTEMI:STEMI	1:69
AWMI+LWMI	30(42.8%)
IWMI excluding RVMI	21(30%)
IWMI+RVMI	19(27.1%)
Killip–Kimball Class	I - 45 (64.3%) II - 15 (21.4%) III - 2 (2.9%) IV - 8 (11.4%)
S.Creatinine (mg/dl) at admission	0.51 ± 0.1 (Range 0.33 - 0.8)
S. Creatinine (mg/dl) at 48h	1.37 ± 0.53 (Range 0.53 - 2.23)
CRS –I incidence	47(67.1%)

LVEF% (Simpsons)	42.7 ± 6.2 (Range 30 – 54)
Mitral E/A Ratio	1.52 ± 0.33 (Range 1.13 - 2.81)
Mitral E/e' Ratio	15.1 ± 3 (Range 7.5 - 22.5)
E deceleration time (EDT)	187.2 ± 22.5 (Range 145 – 236)
RVTAM	1.69 ± 0.23 (Range 0.8 – 2)
RV Systolic S Velocity	0.12 ± 0.02 (Range 0.07 - 0.180)
Revascularization / No Revascularization	66/4
In-Hospital MARCCE	15 (21.4%)

Clinical severity markers demonstrated strong associations with CRS1. Patients presenting with cardiogenic shock exhibited a 100% incidence of CRS1, while those with elevated jugular venous pressure (JVP) had a significantly higher incidence (90% vs. 58%, $p=0.010$). Similarly, diabetes mellitus and anterior wall myocardial infarction were associated with increased CRS1 risk. A graded relationship was observed with Killip class, where higher classes (III and IV) demonstrated near-universal CRS1 occurrence. Importantly, traditional risk factors such as age, sex, hypertension, and dyslipidemia did not show significant associations, suggesting that acute hemodynamic factors outweigh chronic risk profiles in determining renal outcomes during ACS. The binary logistic regression model identifies key predictors of CRS 1, showing that raised JVP showed an adjusted odds ratio (OR) of 9.29 (95% CI 1.17-138.61, $p=0.060$), retaining borderline significance from univariable OR of 6.52 (95% CI 1.64-43.83, $p=0.019$). Diabetes mellitus had an adjusted OR of 5.28 (95% CI 1.07-36.30, $p=0.057$), close to significance following univariable OR of 3.37 (95% CI 1.20-10.25, $p=0.025$). AWMIs had an adjusted OR of 4.77 (95% CI 0.96-26.07, $p=0.060$), with univariable OR of 4.09 (95% CI 1.38-14.07, $p=0.016$), while RVMI showed the strongest adjusted OR of 27.77 (95% CI 3.43-434.27, $p=0.005$) from univariable OR of 5.95 (95% CI 1.49-40.08, $p=0.026$). LVEF less than 40% had an adjusted OR of 14.04 (95% CI 1.76-193.11, $p=0.024$), confirming significant risk from univariable OR of 6.52 (95% CI 1.64-43.83, $p=0.019$). This model highlights RVMI and reduced LVEF as the most robust independent predictors of CRS 1 in acute coronary syndrome with heart failure. (Table 2& Fig. 1)

Table 2: Binary logistic regression model for predictors of CRS1

	CRS I incidence	Odds Ratio (univariable)	Odds Ratio (multivariable)
JVP			
Normal (50)	29(58%)	6.52	9.29
Raised (20)	18(90%)	(1.64-43.83, $p=0.019$)	(1.17-138.61, $p=0.060$)
DM			

No (35) Yes(35)	19(54.3%) 28(20%)	3.37 (1.20-10.25, p=0.025)	5.28 (1.07-36.30, p=0.057)
AWMI+LWMI No (40) Yes (30)	22(55%) 25(83.3%)	4.09 (1.38-14.07, p=0.016)	4.77 (0.96-26.07, p=0.060)
IWMI+RVMI No(51) Yes(19)	30(58.8%) 17(89.5%)	5.95 (1.49-40.08, p=0.026)	27.77 (3.43-434.27, p=0.005)
LVEF >40% (51) <40% (19)	29(58.8%) 18(90%)	6.52 (1.64-43.83, p=0.019)	14.04 (1.76-193.11, p=0.024)

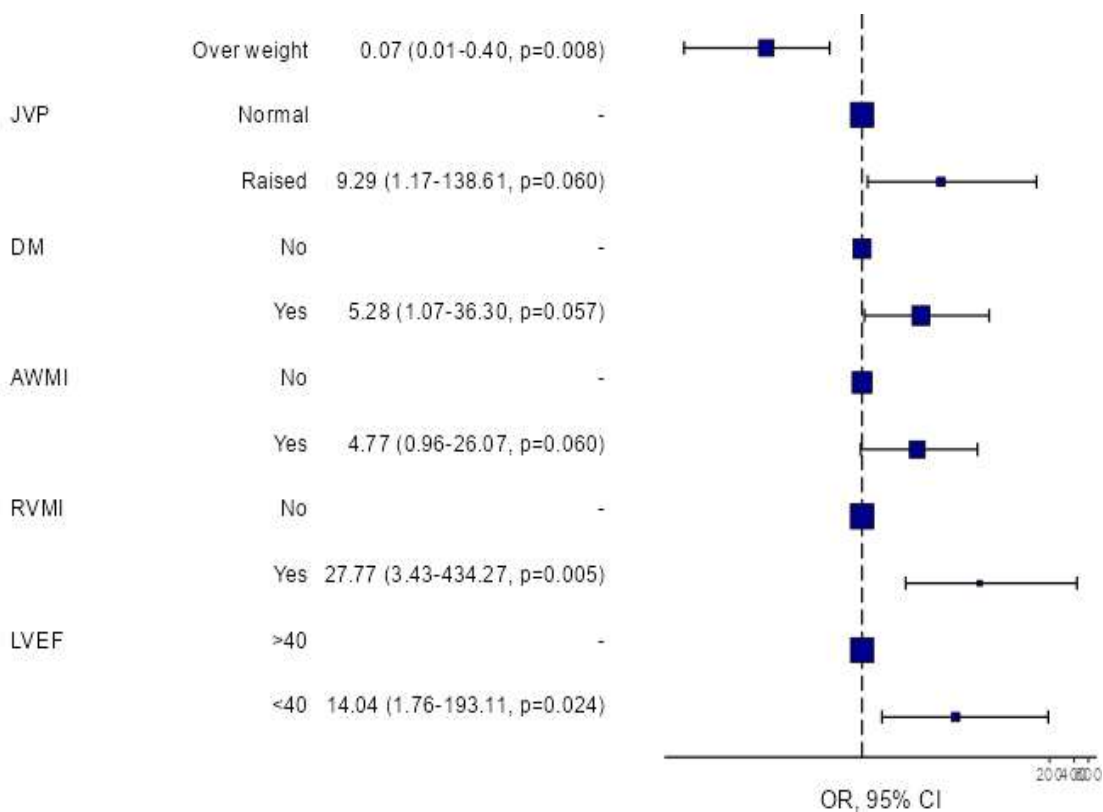


Fig.1: Forest plot-logic regression analysis showing clinical predictors for CRS 1

Echocardiographic analysis revealed that patients who developed CRS1 had significantly impaired systolic and diastolic function. Reduced LVEF (<40%) was strongly associated with CRS1 (90% incidence, $p=0.008$). Tissue Doppler imaging demonstrated lower e' velocities and higher E/e' ratios, indicating elevated left ventricular filling pressures. ROC analysis showed that LVEF had the highest predictive value (AUC 0.72), followed by E/e' ratio and E deceleration time (AUC 0.69 each). Multivariable logistic regression identified right ventricular myocardial infarction (RVMI) as the strongest independent predictor (OR 27.77, $p=0.005$), followed by LVEF <40% (OR 14.04, $p=0.024$) (Table 3). Notably, all in-hospital and follow-up major adverse renal and cardiovascular events (MARCCE) occurred exclusively in patients who developed CRS1, underscoring its prognostic significance.

Table 3: Echocardiographic parameters in predicting Type1 Cardiorenal Syndrome (CRS) with ROC curve and AUC values.

PARAMETER	AUC(PREDICTIVE VALUE)
LVEF%(Simpsons)	0.72
Mitral E/e' Ratio	0.69
E deceleration time(EDT)	0.69
Mitral S'(m/s)	0.68
e' (m/s)	0.67
Mitral E/A Ratio	0.61
RVTAM	0.58
Mitral E (m/s)	0.57
Mitral A(m/s)	0.54
RV Systolic S' Velocity	0.5

DISCUSSION

This study highlights a remarkably high incidence of CRS1 (67.1%) in patients presenting with ACS complicated by heart failure, emphasizing the critical interplay between cardiac dysfunction and renal injury in acute settings. The findings support the evolving paradigm that CRS1 is not solely a consequence of reduced cardiac output but rather a multifactorial process involving both forward failure and venous congestion [1, 2]. While reduced LVEF reflects impaired forward flow and diminished renal perfusion, the strong association of elevated JVP and RVMI underscores the importance of backward failure and increased central venous pressure as key drivers of renal dysfunction. These observations are consistent with previous studies demonstrating that venous congestion is a stronger predictor of worsening renal function than cardiac output alone [6, 7 and 8].

The identification of RVMI as the most powerful independent predictor provides important mechanistic insight. Right ventricular dysfunction leads to elevated central venous pressure, which is transmitted to the renal veins, resulting in increased interstitial pressure, reduced glomerular filtration gradient, and subsequent AKI [15, 16]. This hemodynamic mechanism explains the strong association between raised JVP and CRS1 observed in this study. Additionally, the significant role of diabetes mellitus and elevated urinary albumin highlights the contribution of pre-existing microvascular and endothelial dysfunction, which may reduce renal reserve and increase susceptibility to acute injury [19].

Echocardiographic parameters emerged as valuable tools for early risk stratification. Reduced LVEF and elevated E/e' ratio were strong predictors of CRS1, reflecting the combined effects of systolic dysfunction and elevated filling pressures. The E/e' ratio, in particular, serves as a reliable non-invasive surrogate for left ventricular filling pressure and has been shown to correlate with pulmonary capillary wedge pressure and outcomes in heart failure [17, 18]. The findings support a "dual-hit" hypothesis, where both decreased forward perfusion and increased venous congestion synergistically contribute to renal injury [6, 7]. Importantly, the observation that all adverse outcomes occurred exclusively in CRS1 patients underscores its role as a critical prognostic marker. Previous studies have similarly demonstrated that AKI following ACS is associated with increased mortality and adverse cardiovascular outcomes [5, 20]. Early identification using echocardiography may therefore allow timely intervention, including optimization of volume status, hemodynamics, and renal perfusion.

The predominance of STEMI cases may limit the applicability of the findings to all ACS populations. The use of contrast agent during intervention and its contribution to kidney injury is not considered in this study. Relatively short follow-up period in this may underestimate long-term outcomes.

Conclusion

CRS1 is highly prevalent in ACS with heart failure and strongly predicts adverse outcomes. RVMI and reduced LVEF emerged as key independent predictors, supporting a dual mechanism of reduced perfusion and venous congestion. Early echocardiographic assessment is essential for risk stratification. Limitations include small sample size, single-center design, STEMI predominance, and reliance on non-invasive hemodynamic measures, which may affect generalizability.

References

1. Ronco C, Haapio M, House AA, Anavekar N, Bellomo R. Cardiorenal syndrome. *J Am Coll Cardiol*. 2008;52(19):1527-39.
2. Rangaswami J, Bhalla V, Blair JEA, Chang TI, Costa S, Lentine KL, et al. Cardiorenal syndrome: Classification, pathophysiology, diagnosis, and treatment strategies. *Circulation*. 2019;139(16):e840-e878.
3. Ronco C, McCullough P, Anker SD, Anand I, Aspromonte N, Bagshaw SM, et al. Cardio-renal syndromes: Report from the consensus conference of the Acute Dialysis Quality Initiative. *Eur Heart J*. 2010;31(6):703-11.
4. Cruz DN, Goh CY, Marenzi G, Haapio M, Perazella MA, Bellomo R, et al. Cardiorenal syndrome type 1: Epidemiology and outcomes. *Clin J Am Soc Nephrol*. 2010;5(7):121-26.
5. Anavekar NS, McMurray JJV, Velazquez EJ, Solomon SD, Kober L, Rouleau JL, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med*. 2004;351(13):1285-95.
6. Mullens W, Abrahams Z, Francis GS, Sokos G, Taylor DO, Starling RC, et al. Importance of venous congestion for worsening renal function in advanced decompensated heart failure. *J Am Coll Cardiol*. 2009;53(7):589-96.
7. Testani JM, Chen J, McCauley BD, Kimmel SE, Shannon RP. Potential effects of aggressive decongestion during treatment of decompensated heart failure on renal function and survival. *J Am Coll Cardiol*. 2010;56(15):1213-21.
8. Damman K, Navis G, Voors AA, Asselbergs FW, Smilde TD, Cleland JGF, et al. Worsening renal function and prognosis in heart failure: Systematic review and meta-analysis. *J Am Coll Cardiol*. 2007;49(5):589-96.
9. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth Universal Definition of Myocardial Infarction. *Eur Heart J*. 2019;40(3):237-69.
10. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2018;39(2):119-77.
11. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42(36):3599-726.

12. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl.* 2012;2(1):1-138.
13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults. *J Am Soc Echocardiogr.* 2015;28(1):1-39.
14. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF III, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr.* 2016;29(4):277-314.
15. Goldstein JA. Pathophysiology and management of right ventricular infarction. *J Am Coll Cardiol.* 2002;40(5):841-53.
16. Møller JE, Hillis GS, Oh JK, Reeder GS, Gersh BJ, Pellikka PA. Right ventricular infarction and prognosis after acute myocardial infarction. *Circulation.* 2003;107(22):2789-94.
17. Ommen SR, Nishimura RA, Appleton CP, Miller FA Jr, Oh JK, Redfield MM, Tajik AJ. Clinical utility of Doppler echocardiography and tissue Doppler imaging in estimation of left ventricular filling pressures. *Circulation.* 2000;102(15):1788-94.
18. Dokainish H, Zoghbi WA, Lakkis NM, Al-Bakshy F, Dhir M, Quinones MA, et al. Optimal noninvasive assessment of left ventricular filling pressures. *Circulation.* 2004;109(20):2432-39.
19. Ritz E, Orth SR. Nephropathy in patients with type 2 diabetes mellitus. *N Engl J Med.* 1999;341(15):1127-33.
20. Fox CS, Muntner P, Chen AY, Alexander KP, Roe MT, Cannon CP, et al. Use of evidence-based therapies and outcomes in patients with chronic kidney disease and acute coronary syndromes. *Circulation.* 2010;121(3):357-65.