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The Utility of Renal Artery Doppler Ultrasound in Acute Cardiorenal Syndrome Type 1

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Abstract:

Objectives: The bidirectional relationship between the heart and the kidney is called cardiorenal syndrome (CRS). Many studies revealed an association between renal artery Doppler parameters and acute kidney injury (AKI) occurring in these patients. In this study we investigated the changes of renal artery Doppler parameters with fluid removal. **Methods:** We enrolled patients with CRS type1 admitted in the intensive care unit in Kasr Al Ainy Hospital, Cairo University. Renal artery duplex was done on admission and after 72 hours, to calculate resistivity index (RI), acceleration time (AT) and velocity-time integral (VTI). **Results:** A total of 51 patients met eligibility criteria during the study period. Serum creatinine improved in 38 patients and didn't improve in 13 patients. The renal artery RI, AT, or VTI on day1 and day3 were (0.7 vs 0.7), (48 msec vs 50 msec), (13.3 vs 13) respectively. There was no significant correlation between AKI response on day3 (resolving or not resolving) with the change in renal artery RI, AT, or VTI (p value 0.457, 0.791 and 0.261 respectively). **Conclusion:** The change of renal artery Doppler parameters between day1 and day3 didn't show any correlation with the change of the serum creatinine in patients with CRS type1.

Key words: Renal artery, Doppler, Ultrasound, Cardiorenal syndrome, Acute kidney injury.

Background:

Heart failure and renal impairment usually co-exist, it is reported that about half of patients with HF have some degree of renal impairment and HF is prevalent in up to 50% of patients with renal impairment (1). Renal dysfunction in heart failure (HF) has traditionally been considered to result from decreased renal perfusion and associated neural and hormonal changes. But recently, venous congestion was identified as a major contributor. Systemic congestion develops in patients with heart failure, pulmonary hypertension and with excessive fluid administration. It is a mediator of adverse outcomes in critically ill patients and is a key target in their management (2). Diuresis in patients with right ventricular (RV) dysfunction, despite decreased cardiac output (CO) would lead to a decrease in venous congestion and resultant improvement in renal functions (3). The value of renal ultrasound in these patients is greater when the renal vessels are evaluated by pulsed Doppler techniques (4). Intrarenal Doppler ultrasound (IRD) is a non-invasive bedside tool with good accuracy in defining changes in renal hemodynamics (5). It was suggested that renal artery resistivity index (RI) could be useful in daily clinical practise to better characterise patients with cardio-renal syndrome (6). A high RRI is an independent predictor of WRF at 1 year of follow-up, thus strengthening its role in predicting cardiorenal syndrome progression (7). Identification of changes in renal hemodynamics in patients with cardiorenal disease may aid in the diagnosis and management (8). This study was done to investigate the changes of the renal artery parameters, Resistivity index (RI), acceleration time (AT) and velocity-time integral (VTI), with decongestive therapy in patients with acute cardiorenal syndrome type1.

Methods:*Setting*

A prospective study that included 51 consecutive patients with a provisional diagnosis of cardiorenal syndrome admitted in the medical intensive care unit in Kasr Al Ainy Hospital, Cairo University during a period of 20 months from September 2021 to April 2023. Written consent was obtained for all patients and the study protocol was approved by Cairo university faculty of medicine Research Ethics Committee (MD-312-2021).

Participants

Patients who are over 18 years old, presented with symptoms and signs of ADHF and AKI at admission were enrolled. We excluded patients <18 years, with a diagnosis of obstructive AKI, those having received contrast exposure, known end stage kidney disease on regular hemodialysis or liver cirrhosis, the critically ill who was on either vasopressor medication or mechanical ventilation, and patients without adequate ultrasound windows.

Ultrasound assessment

Ultrasound (US) assessment was performed bedside using the commercially available machine, Philips Affiniti. A phased array transducer was used.

Transthoracic echocardiography was done to evaluate the severity of valvular disease and to measure left ventricle ejection fraction (LVEF) by Simpson's method and tricuspid annular plane systolic excursion (TAPSE).

Renal artery duplex was done on admission and after 48-72 hours of admission. Sampling was done at the level of the arcuate or interlobar arteries, adjacent to medullary pyramids (9) (10). We measured resistivity index (RI), acceleration time (AT) and velocity-time integral (VTI).

Measurements were taken from the segmental arteries in addition to the interlobar (if accessible) from the upper, middle and lower thirds of the kidney and the average of these measurements were taken for each of the three arteries (11). The spectral Doppler renal blood flow velocities were recorded, and the VTI was measured as the area under the outermost portion of the spectral velocity envelope. Doppler velocity-time integral were measured over 3-5 heart beats and average values were recorded. AT is done by placing a caliber on the level at which the gradient begin to rise and finished at the first peak. Renal resistivity index (RRI) is the peak systolic velocity minus end diastolic velocity divided by peak systolic velocity according to the formula: Resistivity index (RI =PSV-EDV/PSV) (12).

Data collection:

Data collection included clinical parameters including body weight, and invasive central venous pressure monitoring (CVP). All diuretic doses, urine output (UOP), fluid balance, and change in body weight (BW) were calculated and documented. We followed serum creatinine level on discharge. Also, mortality and re-hospitalization during the first 90 days of discharge by phone calls.

Statistical analysis

Data management and analysis were performed using Statistical Package for Social Sciences (SPSS) vs. 28. Numerical data were summarized using means and standard deviations or medians and/or ranges, as appropriate. Categorical data were summarized as numbers and percentages. Estimates of the frequency were done using the numbers and percentages. Numerical data were explored for normality using Kolmogorov-Smirnov test and Shapiro-Wilk test. Chi square or Fisher's tests were used to compare between the independent groups with respect to categorical data, as appropriate. McNemar test was done, to compare between two dependent percentages.

Comparisons between two groups for normally distributed numeric variables were done using the Student's t-test while for non-normally distributed numeric variables, comparisons were done by Mann-Whitney test. Comparisons between more than 2 groups were performed by the one-way analysis of variance (ANOVA) for normally distributed variables and Kruskal-Wallis for non-normally distributed variables, then followed by post hoc if needed (Post Hoc comparison was done and P value was adjusted using Bonferroni adjustment). Comparison between two related groups of normally distributed variables was done using paired "t" test, while for non-normally distributed numeric variables, comparisons were done by Wilcoxon test. All tests were two tailed & Probability (p-value) ≤ 0.05 is considered significant and (p-value) ≤ 0.001 is considered highly significant.

Results

Patient characteristics

A total of 51 consecutive patients met eligibility criteria during the study period from September, 2021 till April, 2023. The total number of screened patients was 58, 7 patients were excluded due to technical difficulty, death before completing follow up, or due to withdrawing consents.

Table 1: Baseline characteristics of the involved patients:

	N = 51 (%)
Age (Mean \pm SD)	51 \pm 15
Male	28 (54.9)
BMI>30	26 (51)
Diabetes mellitus	25 (49)
Hypertension	37 (72.5)
Chronic kidney disease (CKD)	8 (15.7)
CKD Stage	
3	6 (75)
4	2 (25)
Acute kidney injury (AKI) staging	
1	31 (60.8)
2	11 (21.6)
3	9 (17.6)
COPD/Asthma	11 (21.6)
Previous stroke	3 (5.9)
Peripheral vascular disease	4 (7.8)
History of cardiac problem	34 (66.7)
Prior heart failure hospitalization	16 (31.4)
CAD	24 (47.1)
Other comorbidities	
No	46 (90.1)
Constrictive pericarditis	1 (2)
Rheumatoid arthritis	1 (2)
SLE	3 (5.9)
Cause of admission/Possible exacerbating factor	
Noncompliance to TTT	22 (43.1)
Uncontrolled HTN	1 (2)
Chest infection	15 (29.4)
Acute myocarditis	3 (5.9)
Lower limb cellulitis	5 (9.8)
Acute coronary syndrome	5 (9.8)
Associated sepsis	27 (52.9)
Severe valvular affection	
No	34 (66.7)
Aortic stenosis	1 (2)
Mitral regurgitation	5 (9.8)
Tricuspid regurgitation	11 (21.6)
	Mean \pm SD

LV Ejection Fraction % D1	39.9 ±13.7
TAPSE cm D1	1.7 ±0.4

SD: standard deviation, CKD: chronic kidney disease, CAD: coronary artery disease, COPD: Chronic obstructive pulmonary disease, HFpEF: Heart failure with preserved ejection fraction, HFrEF : Heart failure with reduced ejection fraction, TTT: treatment, HTN: hypertension, LV: left ventricle, TAPSE: Tricuspid Annular Plane Systolic Excursion

The study involved 51 patients, 28 males and 23 females, with mean age 51 ±15 years. 26 patients were obese (BMI >30 kg/m²), 25 patients were diabetic, 37 patients were hypertensive, Only 8 patients were chronic kidney disease, 6 of them were stage 3, 2 were stage 4, 11 patients were COPD, 3 patients had previous strokes, 4 patients had peripheral vascular disease, 34 patients gave previous history of cardiac problem (heart failure, coronary artery disease), 16 gave history of previous hospitalization due to heart failure. 2 patients had SLE, 1 patient had rheumatoid arthritis. 31 patients were admitted with AKI stage 1, 11 with stage 2, 9 with stage 3 (Table1) (Figure1). Among our included patients, most of them were admitted due to non-compliance to their medications, 22 out of 51 included patients, 15 patients were admitted due to chest infection, the rest were admitted due to acute coronary syndrome, lower limb cellulitis, acute myocarditis or uncontrolled hypertension. Sepsis was found in 27 patients. Tricuspid regurgitation was found in 11 patients, mitral regurgitation was found in 5 patients, aortic stenosis was found in 1 patient. The mean LVEF was 39.9 ±13.7 and the mean TAPSE was 1.7 ±0.4.

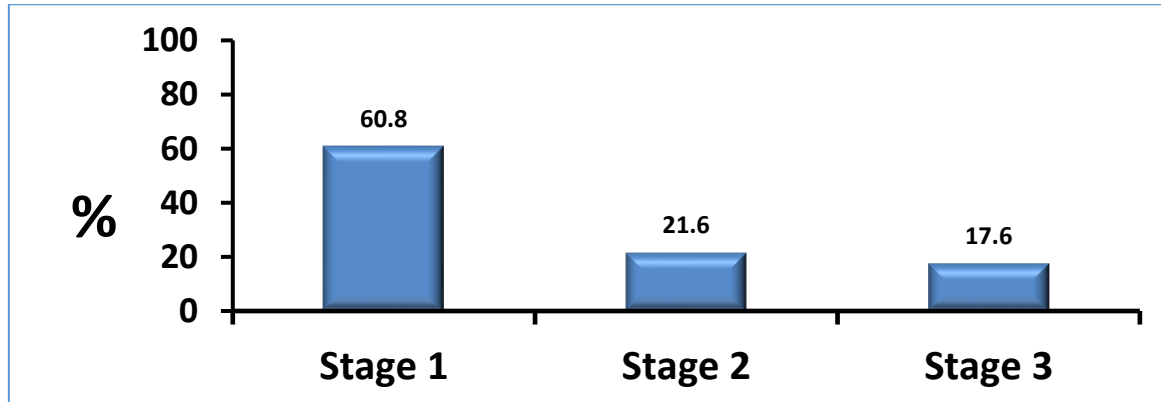


Figure 1: Bar graph representing AKI stage on day 1

Table 2: In hospital drugs & cumulative balance of the involved patients

	N=51 (%)
In hospital beta blocker	8 (15.7)
In hospital Ivabradine	10 (19.6)
In hospital ACE I / ARBs	1 (2)
In hospital loop diuretics shots	20 (39.2)
In hospital loop diuretics infusion	31 (60.8)
In hospital Metolazone	9 (17.6)
In hospital MRA	2 (3.9)
Need for ultra-filtration in 1st 3 days	10 (19.6)

Need for Albumin	2 (3.9)
Dialysis in 1st 3 days	4 (7.8)
Indication for dialysis	
Anuria	3 (75)
Hyperkalemia	1 (25)
Oxygen support O2	14 (27.5)
	Median (range)
Cumulative IV loop diuretic dose (mg)	720 (360-2880)
Cumulative negative balance (ml)	3200 (200-7400)
	Mean \pm SD
Total input (ml)	3025 \pm 481
Total urine output (ml)	6266 \pm 1689

SD: Standard deviation IV: Intravenous

All the patient received intravenous loop diuretics, 20 patients received it by IV shots, 31 received it through IV infusion. Metolazone was used in 9 patients. MRA was used in 2 patients. In the first 3 days of admission, 10 patients underwent ultrafiltration, 4 patients underwent hemodialysis. 14 patients were on oxygen. No patients were on mechanical ventilation, vasopressors or inotropes (Table 2).

Table 3: Clinical, laboratory and renal artery Doppler parameters:

	Mean \pm SD	P value
Body weight D1	85.5 \pm 14	<0.001
Body weight D3	84 \pm 13.5	
CVP D1	20 \pm 3	<0.001
CVP D3	18 \pm 4	
Urea D1	98 \pm 39	<0.001
Urea D3	84 \pm 40	
Creatinine D1	2.6 \pm 1.6	<0.001
Creatinine D3	2.2 \pm 1.5	
CrCl D1	45 \pm 19	<0.001
CrCl D3	58 \pm 25	
	Median (range)	P value
Pulmonary rales D1	43 (84.3)	<0.001
Pulmonary rales D3	27 (52.9)	
Pedal edema D1	39 (76.5)	1
Pedal edema D3	39 (76.5)	
Pleural effusion by US D1	30 (58.8)	0.031
Pleural effusion (US) D3	24 (47.1)	
Ascites by US D1	8 (15.7)	1
Ascites by US D3	8 (15.7)	
NYHA D1		<0.001
3	18 (35.3)	
4	33 (64.7)	

NYHA D3		
2	13 (25.5)	
3	24 (47.1)	
4	14 (27.5)	
Renal A. Resistivity index RRI D1	0.7 (0.6-0.8)	0.054
Renal A. Resistivity index RRI D3	0.7 (0.6-0.8)	
Renal A. Acceleration time AT D1	48 (32-111)	0.200
Renal A. Acceleration time AT D3	50 (33-148)	
Renal A. VTI D1	13.3 (7-24)	0.955
Renal A. VTI D3	13 (8.8-24)	

SD: Standard deviation, P value <0.05 is considered significant, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CVP: Central venous pressure, NYHA: NewYork Heart Association, US: ultrasound, SD: Standard deviation, P value <0.05 is considered significant, P value <0.001 is considered highly significant, CrCl: creatinine clearance, P value <0.05 is considered significant, RA: renal artery, AT: acceleration time, VTI: velocity time integral, RRI renal resistivity index * Data presented as median (range)

On admission, 43 patients had pulmonary rales, 39 had pedal edema, 30 patients had pleural effusion, 8 had ascites. The change in body weight, and CVP between day1 and day3, was highly significant. Also, pulmonary rales, and NYHA score had changed significantly between day 1 and day 3. The change in Urea, Creatinine, and CrCl between day1 and day 3 was highly significant. The renal artery resistivity index (0.7 vs 0.7) on day1 and day3 respectively. Acceleration time (48 msec vs 50 msec) on day1 and day3 respectively. Velocity time integral (13.3 vs 13) on day1 and day3 respectively (Table 3). The mean serum creatinine (2.6 ± 1.6 mg/dl vs 2.2 ± 1.5 mg/dl) on day 1 and day 3 respectively (Figure 2).

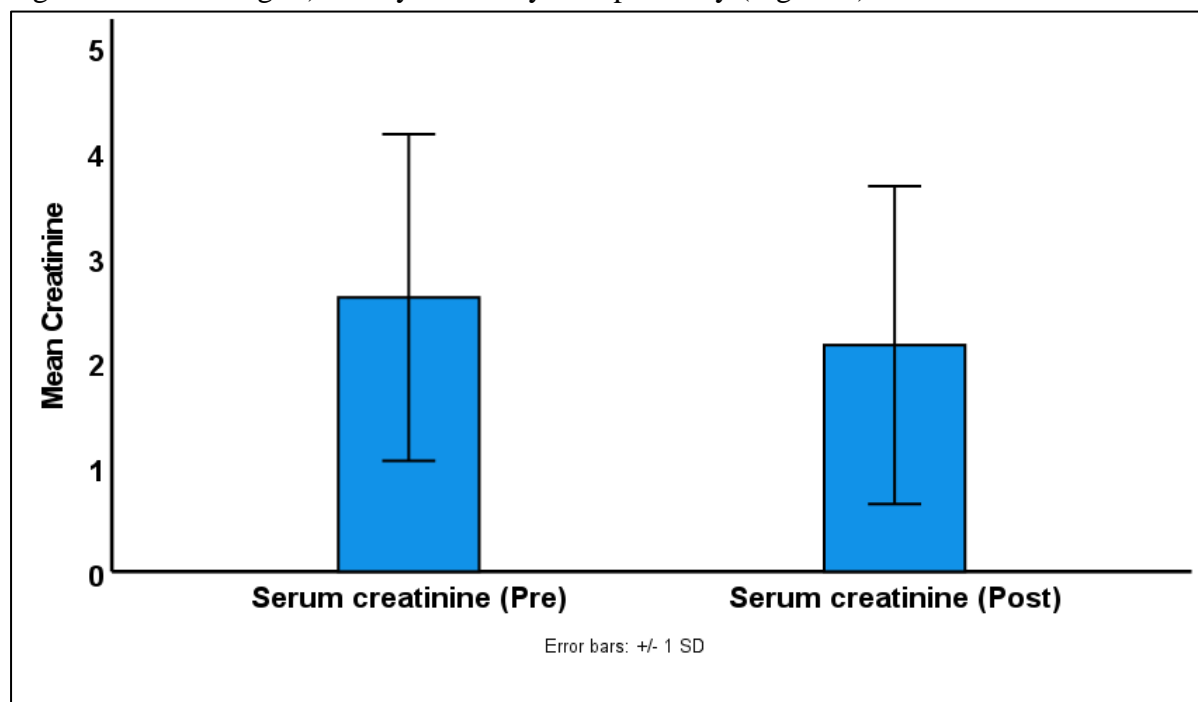


Figure 2: Serum creatinine level on day 1 and day 3 (before and after fluid removal)

Table 4: The change in renal artery Doppler parameters:

	N=51 (%)
Renal A. resistivity index change	
No change	5 (9.8)
Increase	17 (33.3)
Decrease	29 (56.9)
Renal A. Acceleration time AT change	
No change	5 (9.8)
Increase	29 (56.9)
Decrease	17 (33.3)
Renal A. VTI change	
No change	6 (11.8)
Increase	23 (45.1)
Decrease	22 (43.1)

RA: renal artery, AT: acceleration time, VTI: velocity time integral, RRI renal resistivity index. The renal artery resistivity index increased in 17 patients, decreased in 29 patients, but didn't change in 5 patients. Acceleration time increased in 29 patients, decreased in 17 patients, but didn't change in 5 patients. Velocity time integral increased in 23 patients, decreased in 22 patients, but didn't change in 6 patients (Table 5).

Table 5: Comparing AKI response on day3 with the change in renal artery parameters:

	AKI response D3		P value
	Resolving	Not resolving	
	N=38(%)	N=13(%)	
Weight change			
No change	0 (0)	4 (30.8)	
Decrease	38 (100)	5 (38.5)	
Increase	0 (0)	4 (30.8)	
CVP change			
No change	15 (39.5)	7 (53.8)	
Decrease	23 (60.5)	4 (30.8)	
Increase	0 (0)	2 (15.4)	
The change in RRI			
No change	5 (13.2)	0 (0)	0.457
Increase	12 (31.6)	5 (38.5)	
Decrease	21 (55.3)	8 (61.5)	
The change in Renal Artery AT			
No change	3 (7.9)	2 (15.4)	0.791
Increase	22 (57.9)	7 (53.8)	
Decrease	13 (34.2)	4 (30.8)	
The change in Renal Artery VTI			
No change	3 (7.9)	3 (23.1)	0.261

Increase	19 (50)	4 (30.8)	
Decrease	16 (42.1)	6 (46.2)	

P value <0.05 is considered significant, NA: Not applicable, RA: renal artery, AT: acceleration time, VTI: velocity time integral, RRI renal resistivity index.

AKI improved in 38 patients and didn't improve in 13 patients. There was no significant correlation between AKI response on day3 with the change in body weight, change in CVP, change in renal artery resistivity index RI, change in renal artery Acceleration time AT, change in renal artery VTI (Table 5).

Discussion

Type 1 CRS reflects an abrupt worsening of cardiac function leading to acute kidney injury. Biomarkers can contribute to an early diagnosis of CRS and to a timely therapeutic intervention (13). Diuresis is considered to be the main treatment in such patients to decrease the venous congestion and cause improvement in renal functions (3). Evaluation of the renal vessels by pulsed Doppler techniques can add a greater value to the ultrasonographic assessment in these special group of patients (4). Our study included 51 patients admitted with cardiorenal syndrome type 1. Serum creatinine improved in 38 patients and didn't improve in 13 patients. The renal artery resistivity index, acceleration time, and velocity time integral on day1 and day3 were (0.7 vs 0.7), (48 msec vs 50 msec), (13.3 vs 13) respectively. There was no significant correlation between AKI response on day3 (resolving or not resolving) with the change in renal artery RI, AT, or VTI (p value 0.457, 0.791 and 0.261 respectively).

Wallbach M evaluated 35 patients with left ventricular ejection fraction (LV-EF) \leq 35% hospitalized due to ADHF. IRD measurement was performed within the first 48 h of hospitalisation and before discharge. Decongestion strategies were based on clinical judgement according to heart failure guidelines. IRD was used to assess intrarenal venous flow (IRVF) pattern, venous impedance index (VII) and resistance index (RI). Laboratory analyses included plasma creatinine, eGFR and albuminuria. At discharge, there was a significant reduction of VII from a median of 1.0 (0.86–1.0) to 0.59 (0.26–1.0) ($p < 0.01$) as well as improvement of IRVF pattern categories ($p < 0.05$) compared to inclusion. Plasma creatinine and RI remained unchanged ($p = 0.73$; $p = 0.43$). So, in contrast to the observed changes of parameters of the renal venous system, RI as a parameter of the renal arterial system remained unchanged during recompensation (14). Çakal B evaluated 64 cases of CRS type 1 by serial measurements of the renal venous impedance index (VII) and resistive index (RI). A total of 30 patients who had creatinine improvement with diuresis (group 1) and 34 patients without any improvement (group 2) were analyzed. Patients in group 1 had higher median VII and ARI (VII, 0.86 versus 0.66; $P < .001$; ARI, 0.78 versus 0.65; $P < .001$) on admission. A high ARI on admission (odds ratio, 6.25; 95% confidence interval, 1.84–14.3; $P = .003$) predicted the improvement of serum creatinine levels with diuretic therapy independent of confounding factors in patients with CRS type 1. So, they concluded that renal vascular Doppler parameters might offer guidance on the diagnostic and therapeutic strategies in prescribing decongestive therapy for decompensated heart failure (15).

Ciccione MM et al enrolled 250 outpatients with CHF in stable clinical conditions and on conventional therapy. Renal artery pulsed Doppler flow recording was performed.

During follow-up (17.8±9.9 months), 37 patients experienced heart failure worsening.

RRI $\geq 75\%$ was associated with events at univariate as well as at multivariate analysis. So, concluded that RRI had a separate role in predicting the evolution of heart failure in CHF patients (6).

Lacoviello M et al, found that renal arterial resistivity index (RRI) can reflect abnormalities in the renal blood flow, and quantification of arterial renal perfusion provides a novel parameter that independently predicts the WRF in CHF patients (7). Mostafa A et al suggested that intrarenal haemodynamics, particularly renal AT and RI, are independent parameters that can help identify ADHF patients undergoing diuretic medication who are at increased risk for WRF (11). Both studies evaluated the changes on admission and discharge but in our cohort, the correlation with renal function improvement was poor, this may be due to the short time interval (72 hours) between the first and second renal artery Doppler evaluations.

The main finding of our study is that RRI remained unchanged during decongestive therapy in our cohort between day1 and day3. The evaluation of RRI guided therapy in larger longitudinal studies in patients with ADHF is needed to evaluate its impact on cardiorenal outcome.

Limitations

Some limitations of the present study need to be considered. The primary limitations of the study are its single-center design and small sample size, and the lack of long-term follow-up. Also, it was conducted in a specific group of patients with AKI (cardiorenal syndrome). So, our findings need to be confirmed by multi-center investigations including more patients.

Conclusion

The change of renal artery Doppler parameters between day1 and day3 didn't show any correlation with the change of the serum creatinine in patients with CRS type1.

Abbreviations

ADHF: Acutely decompensated heart failure.

CRS: cardiorenal syndrome

CO: cardiac output

AKI: Acute kidney injury.

CVP: Central Venous Pressure.

SOFA: Sequential organ failure assessment.

ICU: Intensive care unit.

2D: Two dimensional.

BW: Body weight.

UOP: Urine output.

mL: milliliter.

LV: Left ventricle.

RV: Right ventricle.

LVEF: Left ventricle ejection fraction.

TAPSE: Tricuspid annular plane systolic excursion

RA: Renal artery

AT: Acceleration time

VTI: Velocity time integral

RRI: Renal resistivity index.

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None

Contributions:

Eslam Abu-Naeima designed and conducted the study, Mahmoud Amin Abu-Sheaishaa Shalaby performed the echocardiographic evaluation, Ghada Ayeldeen performed the biochemical analysis, Ahmed Fayed, Moataz Fatthy contributed to the design of the study and reviewed the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate:

Written consent was obtained for all patients and the project was approved by Cairo university faculty of medicine Research Ethics Committee (MD-312-2021).

Consent for publication:

Not applicable.

Competing interests:

The authors have no conflict of interest to declare.

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