

REVIEW

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# Evaluation of ventricular systolic dysfunction as a risk factor for acute kidney injury in intensive care unit

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## Abstract

**Background:** Heart failure (HF) is a major health problem. Cardiac and renal diseases interact in a complex bidirectional manner in both acute and chronic settings. Renal dysfunction in the setting of heart failure, termed the cardio renal syndrome (CRS), has been considered consequence of left ventricular dysfunction (LVD), whereby decreasing cardiac output (COP) results in renal under perfusion and consequent decreased glomerular filtration rate (GFR).

**Main body of the abstract:** This study showed that 500 patients were admitted to internal care unit (ICU), and out of them, 100 (20%) patients developed acute kidney injury (AKI) while 400 (80%) patients did not develop AKI. It is also showed that 67 (67%) of those with AKI and 100 (25%) of those with no-AKI had baseline ventricular systolic dysfunction, left ventricular dysfunction (LVD), right ventricular dysfunction (RVD), and biventricular dysfunction (BIVD) presented in 23 (23%), 16 (16%), and 28 (28%) patients of AKI group, respectively, and presented in 60 (15%), 30 (7.50%), and 10 (2.50%) patients, respectively, in patients without acute kidney injury (AKI)

**Short conclusion:** Our study revealed that AKI has highest incidence in patient with biventricular dysfunction followed by left ventricular dysfunction and lastly those with right ventricular dysfunction.

**Keywords:** Acute kidney injury, Ventricular systolic dysfunction, Chronic kidney disease

## Background

Renal dysfunction in the setting of heart failure (HF), termed as cardio renal syndrome (CRS), has traditionally been considered a consequence of left ventricular dysfunction (LVD), whereby decreasing cardiac output (COP) results in renal under perfusion and consequent decreased glomerular filtration rate (GFR) [1].

However, emerging data have highlighted the importance of the right ventricle; right ventricular dysfunction can lead to renin-angiotensin aldosterone system (RAAS) activation, sodium retention, and volume overload. With the development of venous congestion in renal dysfunction, peripheral edema and increased central venous pressure (CVP) would

be associated with a higher risk of acute kidney injury (AKI) [2].

Cardio renal syndromes (CRS) are broadly divided into two main groups, cardio-renal and reno-cardiac CRS, on the basis of the premium maven of disease (cardio or renal). Both cardio-renal and reno-cardiac CRSs are then divided into acute and chronic, according to disease's onset. Type 5 of CRS is defined as simultaneous cardio-renal involvement induced by systemic disease [3].

## Methods

### Study design

A randomized prospective cohort study was performed at intensive care units (ICUs) of Internal Medicine Department, from January 2018 till 2019.

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### Subject

The study included 500 patients that were admitted to ICU for different causes. Patient with end stage renal disease (ESRD), chronic kidney disease (CKD), AKI with post-renal cause, AKI due to other causes rather than ventricular dysfunction, and lastly cirrhotic patient were excluded from this study.

### Biochemical assay

All patients included in the study were subjected to careful history taking, clinical examination, and different laboratory investigations which include

- Random blood glucose, hemoglobin, blood urea, and serum creatinine.
- The baseline value of the estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (CKD\_EPI).

### Cardiac investigations

- Twelve lead ECG, cardiac enzyme evaluation (total creatine phosphokinase CK-MB, lactate dehydrogenase, and troponin I).
- Echocardiography (EF % ejection fraction, TAPSE (tricuspid plane annular systolic excursion). PWT: posterior wall thickness; LVESD: left ventricular end systolic diameter; LVEDD: left ventricular end diastolic diameter; LAVI: left atrial volume index). According to American society of Echocardiology (ASE) guidelines define an abnormal EF as < 55%, with the cutoffs for moderately abnormal and severely abnormal at 44% and 30%, respectively. TAPSE: of < 17 mm indicates RV dysfunction [4].
- The primary outcome will be AKI during the first 7 days of ICU care, as defined by an increase of  $\geq 0.3$  mg/dl in serum creatinine within 48 h of ICU admission, an increase of  $\geq 50\%$  within 7 days of ICU admission, or acute dialysis, in keeping with the kidney disease improving global outcomes guidelines KDIGO [5].

### Statistical analysis of data

Data was collected and analyzed those using SPSS (Statistical Package for the Social Science, version 20, IBM, and Armonk, NY). Continuous data was expressed in form of mean  $\pm$  SD or median (range) while nominal data was expressed in form of frequency (percentage).

Chi-squared test was used to compare the nominal data of different groups in the study while Student's t test was used to compare mean of different two groups.

Multivariate regression analysis was used to determine the independent risk factors for prediction of development

of AKI. Level of confidence was kept at 95% and hence, *P* value was significant if < 0.05.

### Results

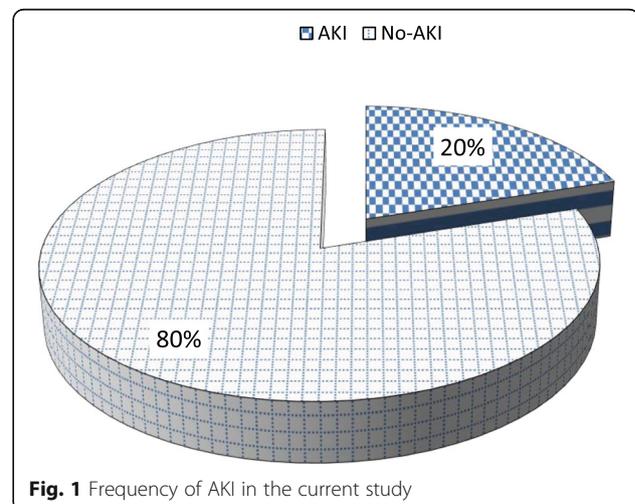
Our study showed that 500 patients were admitted to ICU, out of them; 100 (20%) patients developed AKI while 400 (80%) patients did not develop AKI. Our study revealed that mean age of patients with AKI was  $65.78 \pm 12.98$  years and majority (70%) of them was males with mean body mass index were  $25.67 \pm 2.34$  kg/m<sup>2</sup>. In case of those with no-AKI, mean age was  $55.87 \pm 11.10$  years with mean body mass index was  $26.09 \pm 3.30$  kg/m<sup>2</sup> and also, majority (60%) of them was males (Fig. 1, Table 1).

It was noticed that in majority of cases (70% of those with AKI and 69% of those with no-AKI) was admitted secondary to acute coronary syndrome. Pulmonary embolism and cerebrovascular stroke were the cause of admission in 25 (25%) and 5 (5%) patients with AKI, respectively, and 84 (21%) and 40 (40%) patients with no-AKI, respectively (Table 2).

Also, it was noticed that both groups of patients had insignificant differences as regards baseline urea, creatinine, and estimated glomerular filtrate (eGFR). Serum creatinine and blood urea were significantly higher during 3rd and 5th day in patients with AKI than those without AKI while eGFR was significantly higher among patients with no-AKI during 3rd and 5th day than those with AKI (Table 3)

As regards echocardiographic parameters, our study showed that patients with AKI had significantly lower ejection fraction in comparison to those with no-AKI ( $49.11 \pm 2.34$  vs.  $54.78 \pm 2.78$ ; *P* < 0.001). It was noticed that left atrial diameter and volume and left ventricular end diastolic/systolic diameter were significantly higher in patients with AKI (Table 4).

As regards ventricular dysfunction, it was noticed that 67 (67%) of those with AKI and 100 (25%) of those with



**Fig. 1** Frequency of AKI in the current study

**Table 1** Patient characteristics of studied patients

	AKI (n = 100)	No-AKI (n = 400)	P
Age (years)	65.78 ± 12.98	55.87 ± 11.10	0.04 S
Sex			0.45 NS
Male	70 (70%)	240 (60%)	
Female	30 (30%)	160 (40%)	
Body mass index (kg/m <sup>2</sup> )	25.67 ± 2.34	26.09 ± 3.30	0.33 NS
Smoking	48 (12%)	10(10%)	0,12NS
Previous admission	33 (33%)	84 (21%)	0.04 S
Residence			0.09 NS
Rural	66 (66%)	268 (67%)	
Urban	34 (34%)	132 (33%)	

S significant, value &lt; 0.05

NS non-significant, value &gt; 0.05

no-AKI had baseline ventricular dysfunction. Right ventricular dysfunction (RVD), left ventricular dysfunction (LVD), and biventricular dysfunction (BiVD) presented in 16 (16%), 23 (23%), and 28 (28%) patients of AKI group, respectively, and presented in 30 (7.50%), 60 (15%), and 10 (2.50%) patients, respectively (Table 4).

In our study, it was found that the incidence of the stages of acute kidney injury was 55 (55%), 25 (25%), and 20 (20%) stage I, II, and III, respectively. Also, it was found that no significant differences between different stages of AKI as regards echocardiographic parameters with exception of ventricular dysfunction where majority of patients (50%) with grade III AKI had biventricular dysfunction (Figs. 2 and 3)

## Discussion

Our study included 500 patients, out of which 100 (20%) patients developed AKI while 400 (80%) patients did not develop AKI. As shown in Fig. 1, and disagreed with that found by Stanojević et al. (2012) [6], 42.2% of patients had AKI. Moreover, Waldum et al. (2010) [7] found that AKI (eGFR < 60 ml/min) was present in 44.9% of patients as it was a large cross-sectional study.

We found that patients with AKI had significantly higher mean age in comparison to those without AKI. This is in agreement with the study by Roik et al. (2006) [8]. Various studies have shown a clear age-dependent

**Table 2** Causes of admission in studied patients based on development of acute kidney injury

Causes of admission	AKI (n = 100)	No-AKI (n = 400)	P
Acute coronary syndrome	70 (70%)	276 (69%)	0.09 NS
Pulmonary embolism	25 (25%)	84 (21%)	0.09 NS
CVS	5 (5%)	40 (10%)	0.09 NS

Data expressed as frequency (percentage). P value was significant if &lt; 0.05. non-significant if &gt; 0.05

AKI acute kidney injury, CVS cerebrovascular stroke

**Table 3** Kidney function tests in studied patients based on development of acute kidney injury

Variables	AKI (n = 100)	No-AKI (n = 400)	P
<b>Creatinine (mg/dl)</b>			
Baseline	0.98 ± 0.11	0.99 ± 0.10	0.98 NS
At 3rd day	1.22 ± 0.22	1.01 ± 0.11	< 0.001 S
At 5th day	1.78 ± 0.44	1.02 ± 0.12	< 0.001 S
<b>Urea (mg/dl)</b>			
Baseline	12.45 ± 3.45	11.34 ± 2.45	0.45 NS
At 3rd day	24.78 ± 5.55	10.14 ± 4.44	< 0.001 S
At 5th day	33.78 ± 6.55	11.56 ± 3.45	< 0.001 S
<b>eGFR (ml/min/1.73 m<sup>2</sup>)</b>			
Baseline	107.98 ± 10.44	105.5 ± 5.23	0.09 NS
At 3rd day	88.45 ± 2.45	102.45 ± 3.45	< 0.001 S
At 5th day	65.98 ± 3.45	103.78 ± 2.22	< 0.001S

Data was expressed in form of mean (SD). P value was significant if &lt; 0.05

AKI acute kidney injury, eGFR estimated glomerular filtration rate, S significant, NS non-significant

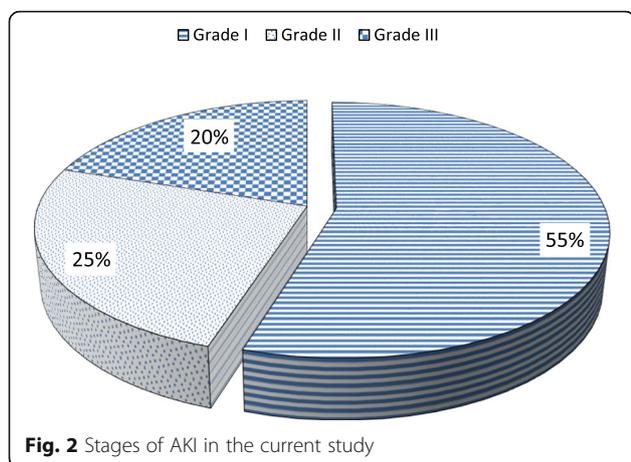
relationship between AKI and older age. This could be attributed to physiological reduction of eGFR with aging [9].

Our present study revealed that frequency of AKI was insignificantly higher among male patient. It was previously reported that male patients had consistently predominated in reports on the AKI incidence which

**Table 4** Echocardiography in studied patients based on development of acute kidney injury

Variables	AKI (n = 100)	No-AKI (n = 400)	P
<b>Ejection fraction (%)</b>	49.11 ± 2.34	54.78 ± 2.78	< 0.001 S
<b>Left atrial diameter (cm)</b>	4.98 ± 0.68	3.01 ± 0.65	0.03 S
<b>Left atrial volume (cm<sup>3</sup>)</b>	39.21 ± 2.62	29.45 ± 3.33	0.01 S
<b>LAVI (cm<sup>3</sup>/mm<sup>2</sup>)</b>	13.94 ± 1.34	11.56 ± 2.30	0.45 NS
<b>PWT (mm)</b>	8.51 ± 1.07	8.78 ± 2.11	0.56 NS
<b>LVEDD (mm)</b>	39.68 ± 5.98	31.04 ± 3.30	< 0.001S
<b>LVEDD (mm)</b>	53.21 ± 5.91	43.76 ± 3.33	< 0.001S
<b>TAPSE (mm)</b>	16.78 ± 3.33	13.45 ± 2.34	< 0.001S
<b>Ventricular function</b>			< 0.001S
Normal biventricular function	33 (33%)	300 (75%)	
Right ventricular dysfunction	16 (16%)	30 (7.50%)	
Left ventricular dysfunction	23 (23%)	60 (15%)	
Biventricular dysfunction	28 (28%)	10 (2.50%)	

Data was expressed in form of mean (SD). P value was significant if &lt; 0.05 AKI acute kidney injury, PWT posterior wall thickness, LVEDD left ventricular end systolic diameter, LVEDD left ventricular end diastolic diameter, LAVI left atrial volume index, TAPSE tricuspid plane annular systolic excursion, S significant, NS non-significant



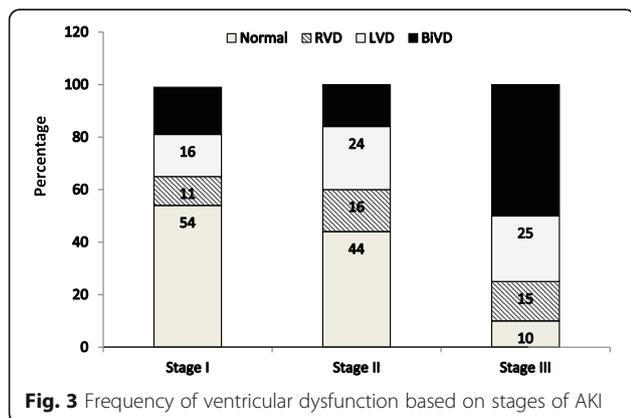
**Fig. 2** Stages of AKI in the current study

may be explained by a higher prevalence of smoking and some other risk factors among males [10].

Also, Collins et al. (2011) [11] showed that men were more likely to develop incident of AKI than women. Mallhi et al. (2015) [12] stated that frequency of AKI among males is secondary to males are usually have better access to health care explaining the higher reported incidence of AKI among males.

In our study, patients with AKI had significantly lower ejection fraction in comparison to those with no-AKI. It was noticed that left atrial diameter and volume, TAPSE, and left ventricular end diastolic/systolic diameter were significantly higher in patients with AKI. Tandon et al. (2013) [13] concluded that lower RV longitudinal function (evaluated with TAPSE) was significantly associated with AKI development during a 3-day follow-up.

As previously described, patients with right ventricular dysfunction have a higher risk of AKI due to raised central venous pressure and low cardiac output [14]. As regards frequency of ventricular dysfunction based on AKI in our study, it was noticed that frequency of ventricular dysfunction was more common among those with AKI.



**Fig. 3** Frequency of ventricular dysfunction based on stages of AKI

This agreed with a study done by Chen et al. (2017) [15] which included 1879 critically ill patients who underwent echocardiography within 24 h of ICU admission, 21% ( $n = 388$ ), 9% ( $n = 167$ ), and 13% ( $n = 252$ ) had isolated right ventricular dysfunction (ILVD), isolated left ventricular dysfunction (IRVD), and BiVD, respectively.

Also, Chen et al. (2017) [15] showed that pulmonary embolism was more common in patients with IRVD (16%) than in those with other forms of ventricular dysfunction, whereas a diagnosis of myocardial infarction was seen in almost 36% of patients with ILVD. Blood pressure was lowest and admission serum creatinine level was highest in those with BiVD.

This in contrast with our study, as it was performed in tertiary center with large number of patients admitted with acute coronary syndrome, so we found that majority of cases (70% of those with AKI and 69% of those with no-AKI) was admitted secondary to acute coronary syndrome.

In our study, we showed that majority of patients (50%) with grade III AKI had biventricular dysfunction. In contrast with our study, Chen et al. 2017 [15] showed AKI tended to be more severe with both IRVD and BiVD. Stage III AKI occurred in 9% ( $n = 15$ ) and 10% ( $n = 26$ ) of patients with IRVD and BiVD, compared with 5% ( $n = 20$ ) and 7% ( $n = 78$ ) of patients with ILVD and normal biventricular function, respectively. This may be secondary to different sample size, selection bias, and/or lost to follow-up

The main limitations of this study include (1) not performing survival analysis of the enrolled patients, (2) short-term follow-up of patients even those who developed AKI, (3) AKI diagnosis was made by serum creatinine changes, although there might be patients who suffered some degree of kidney damage without having elevated creatinine values, and (4) it was done in only one center.

### Conclusion

AKI is common in patients with ventricular dysfunction. Echocardiography is a simple non-invasive tool that could be used for early detection of AKI among susceptible patients in ICU.

### Abbreviations

HF: Heart failure; CRS: Cardiorenal syndrome; LVD: Left ventricular dysfunction; COP: Cardiac output; GFR: Glomerular filtration; VSD: Ventricular systolic dysfunction; ICU: Intensive care unit; AKI: Acute kidney injury; CVP: Central venous pressure; AKI: Acute kidney injury; CKD: Chronic kidney disease; ESRD: End stage renal disease; SD: Standard deviation

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**Authors' contributions**

LA made substantial contributions to the design of the work, the acquisition, analysis, interpretation of data, and was a major contributor in revising the manuscript. AIK made substantial contributions to the design of the work and supervising the work. FRE is the corresponding author, has a major role in collecting the data and laboratory investigations of the patients in the study, had a major role in writing the manuscript, and had a major role in doing the statistical analysis of the data. All authors have read and approved the 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.

**Declarations****Ethics approval and consent to participate**

The study protocol was approved by the Ethics Review Board of Faculty of Medicine, Assiut University, and informed written consent was obtained from all participants according to the Declaration of Helsinki. The committee's reference number is not available.

**Consent for publication**

Not applicable

**Competing interests**

The authors declare that they have no competing interests.

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