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# Non-invasive Hemodynamic Monitoring of Fluid Resuscitation in Cirrhotic Patients with Acute Kidney Injury

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## Abstract

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**BACKGROUND:** Fluid management of patients with liver cirrhosis and acute kidney injury (AKI) is a complex problem requiring accurate assessment of the intravascular volume status and the cause of the AKI. Echocardiography used in various hemodynamic monitoring as a quick, easy, bedside, and non-invasive tool with great sensitivity.

**AIM:** This study aims to evaluate echocardiography as a non-invasive hemodynamic monitoring tool for the assessment of volume status and cardiac function before and after volume expansion in patients with liver cirrhosis presented by AKI.

**PATIENTS AND METHODS:** This study included 120 patients with liver cirrhosis and AKI. All patients were subjected to clinical evaluation, laboratory assessment of kidney and liver functions, and echocardiographic assessment of inferior vena cava (IVC) collapsibility index, left ventricular outflow tract velocity time integral (LVOT VTI) variability index, and cardiac output (CO).

**RESULTS:** Comparison between responders and non-responders to volume resuscitation regarding the echocardiographic data showed that responders had significantly higher IVC collapsibility index, LVOT VTI variability index, and % of CO increase. IVC collapsibility index and LVOT VTI variability index showed good predictive value of fluid responsiveness.

**CONCLUSIONS:** The use of echocardiography is a good tool for hemodynamic monitoring of fluid resuscitation in cirrhotic patients with AKI. The use of echocardiography has limited the use of central venous line only to patients with hemodynamic instability requiring vasoactive support.

## Introduction

Management of cirrhotic patients admitted to intensive care unit (ICU) constitutes a special challenge due to the high morbidity and mortality rates usually encountered with this population. They have significant alterations in their immunological, coagulation, and hemodynamic functions which add to the difficulty of management [1], [2]. Hemodynamic changes include portal hypertension, systemic vasodilation, and hyperdynamic circulation which subsequently result in deteriorated renal and cardiac functions [3].

Acute kidney injury (AKI) is a common life-threatening complication in cirrhotic patients. It is mostly attributed to pre-renal causes, hepatorenal syndrome (HRS), or acute tubular necrosis [4], [5]. Considering the significant hemodynamic changes in cirrhotic patients with AKI, different types of AKI in those patients can be predicted. Among the various methods of hemodynamic monitoring, echocardiography monitoring proved to be more efficient when compared with other methods, for example, central venous pressure (CVP) monitoring [6]. However, value of this

utility in the context of AKI in cirrhotic patients is rarely discussed in the literature.

The present study aims to evaluate the use of echocardiography as a non-invasive hemodynamic monitoring tool for the assessment of volume status and cardiac function before and after volume expansion in patients with liver cirrhosis presented by AKI.

## Patients and Methods

### Study design and enrollment criteria

The present study prospectively recruited a cohort of 40 cirrhotic patients with AKI admitted to the critical care department at Theodor Bilharz Research Institute, Cairo, Egypt. The study protocol was approved by the local ethical committee.

Patients were included in the study on the basis of Child–Turcotte–Pugh classification for end-stage liver disease and AKI network (AKIN) classification for AKI [7]. Exclusion criteria included pregnancy, volume

expansion before echocardiography, portal vein thrombosis, tense ascites, transjugular intrahepatic portosystemic shunt, mechanical ventilation, aortic stenosis, dysrhythmia, heart failure, pulmonary hypertension, and chronic renal failure.

### **Basic evaluation**

All patients were subjected to careful history taking, thorough clinical examination and routine laboratory assessment. HRS was diagnosed according to the following criteria:

1. Liver cirrhosis with ascites.
2. Serum creatinine >1.5 mg/dL.
3. Absence of shock state.
4. No improvement of serum creatinine (decrease to a level of 1.5 mg/dL or less) after at least 2 days of diuretic withdraw and volume expansion with albumin (the recommended dose of albumin is 1 g/kg of body weight per day up to a maximum of 100 g/d).
5. No current or recent exposure to nephrotoxic drugs and absence of parenchymal disease as indicated by proteinuria >500 mg/d, microscopic hematuria [8].

### **Intra-abdominal pressure assessment (IAP)**

IAP was assessed indirectly through indwelling urinary catheter after instillation of 25 mL of saline into the bladder then measuring by CVP ruler 60 s at the end of expiration in supine position. Normal IAP is 5–7 mmHg up to 10 mmHg in critically ill adult patients [9].

### **Fluid challenge**

Fluid challenge was performed by 500 ml crystalloid (NaCl 0.9%) over 20–30 min [10].

### **Echocardiographic assessment**

Echocardiographic assessment was performed for all participants and included:

#### *Inferior vena cava (IVC) collapsibility index*

IVC diameter was measured by transthoracic echocardiography by visualizing the IVC as it entered the right atrium (subcostal window, long-axis view). The M-mode cursor was used to create a time-motion image of the IVC diameter just proximal to the junction of hepatic vein that lies approximately 0.5–0.3 cm proximal to the ostium of the right atrium perpendicular to IVC. IVC diameters were collected over a 20 s period of spontaneous respiration, the maximum and minimum intraventricular conduction delays were measured.

IVC Collapsibility Index=(IVCD MAX-IVCD MIN)/IVCD MAX×100.

IVC collapsibility index more than or equal to 12% considered fluid responsiveness.

#### *Left ventricular outflow tract velocity time integral (LVOT VTI) variability index*

LVOT VTI was obtained by visualizing the LVOT (apical window, 5-chamber view). The pulsed wave Doppler cursor was placed in the middle of the LVOT just adjacent to the aortic valve. The largest and smallest waveforms were collected over a 20 s period of spontaneous respiration.

LVOT VTI variability index =  $\{(VTI_{max} - VTI_{min}) / [(VTI_{max} + VTI_{min}) / 2] \times 100\}$

LVOT VTI variability index more than or equal to 12% considered fluid responsiveness.

#### *Cardiac output (CO)*

We measured CO before and after fluid challenge; then, the percentage of increase in CO was calculated.

$CO = (SV \times HR) / 1000$

Fluid responsiveness defined as increase in CO more than or equal to 15%.

### **Statistical analysis**

Data were statistically analyzed using the Statistical Package for the Social Sciences (IBM, USA) version 23. The quantitative data were presented as mean and standard deviations or median and interquartile range. Qualitative data were presented as number and percentages. The comparison between two independent groups with qualitative data was done using Chi-square test or Fisher's exact test while comparison between quantitative data was done by independent t-test or Mann-Whitney U-test as appropriate. The comparison between paired quantitative variables was achieved using paired t-test or Wilcoxon rank test. Receiver operator characteristic test was used to determine diagnostic test sensitivity and specificity.  $p < 0.05$  was considered statistically significant.

## **Results**

In the present study, fluid responsiveness was achieved in 75 patients (62.5%) with pre-renal azotemia with an improvement of AKI after correction of the intravascular volume status. Forty-five (37.5%) patients were fluid non-responsiveness and fulfilled the

criteria for HRS. Hence, we divided our studied patients two groups:

Group 1: Patients with pre-renal azotemia.

Group 2: Patients with HRS.

Comparison between both groups regarding the various clinical variables revealed that Group 1 patients had significantly better AKIN staging and better Child–Pugh scores (Tables 1 and 2).

**Table 1: Child–Pugh classification of studied group**

		Group 1 no.=75 (%)	Group 2 no.=45 (%)	Test value	p-value
Child	B	33 (44.0)	3 (6.7)	18.667	0.000
	C	42 (56.0)	42 (93.3)		

Comparison between both groups regarding the echocardiographic data showed that Group 1 patients had significantly higher IVC collapsibility index, LVOT VTI variability index, and % of CO increase (Table 3).

**Table 2: AKIN criteria**

AKIN	Group 1 no.=75 (%)	Group 2 no.=45 (%)	Test value	p-value
1	48 (64.0)	12 (26.7)	43.594	0
2	27 (36.0)	12 (26.7)		
3	0 (0.0)	21 (46.7)		

AKIN: Acute kidney injury network.

IVC collapsibility index, LVOT VTI variability index, and % of CO increase showed good predictive value of fluid responsiveness while EF failed to show such value (Table 4, Figures 1-3).

As regard the need for central venous line (CVL) insertion, the use of echocardiography allows to avoid unduly use of central venous catheter in 87 patients (72% of the cases) and hence its complications (Table 5).

Comparison between both groups regarding the in-hospital mortality data showed that Group 2 patients had significantly higher in-hospital mortality (Table 6).

## Discussion

Management of cirrhotic patients with AKI is a complex issue that depends mainly on accurate assessment of intravascular volume status [11]. This study was designed to assess the non-invasive hemodynamic monitoring using echocardiography in evaluation of volume status before and after volume resuscitation in patients with liver cirrhosis presented with AKI.

**Table 3: Echocardiographic measures of the studied groups**

Hemodynamic parameter	Fluid responsiveness			t-value	p-value
	All patients no.=120	Group 1 no.=75	Group 2 no.=45		
IVC collapsibility index median (IQR)	35.5 (10–43.5)	40 (37–47)	8 (4–10)	–9.064	< 0.001
LVOT VTI variability index median (IQR)	22 (20–23)	22.6 (22–23)	19.4 (18.7–21)	–6.568	< 0.001
CO increase (%) median (IQR)	9.32 (4.87–20.46)	16.56 (8.17–23.08)	0.58 (0–8.89)	–6.613	< 0.001

CO: Cardiac output; LVOT VTI: Left ventricular outflow tract velocity time integral; IVC: Inferior vena cava.

The reported causes of AKI in the present study include pre-renal azotemia (62.5%) and HRS (37.5%). Matching with our result, Warner *et al.* [12] who studied AKI in 152 hospitalized cirrhotic patients with liver cirrhosis found that 70% of the patients had pre-renal azotemia.

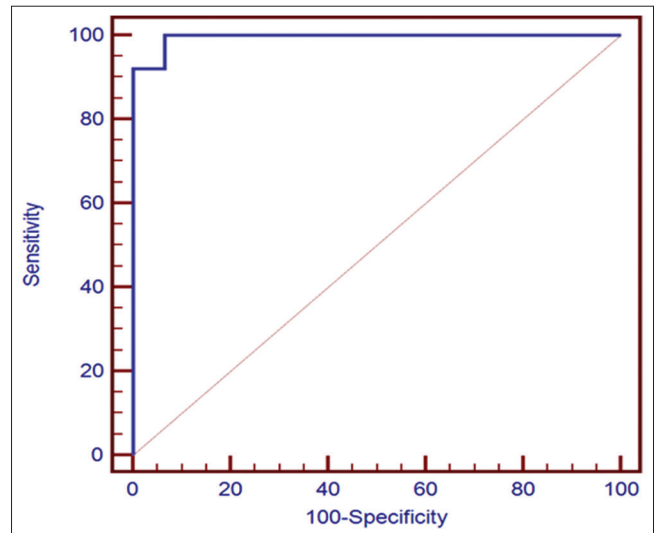


Figure 1: Sensitivity and specificity of inferior vena cava collapsibility index

Fluid responsiveness of these patients was assessed using two dynamic echocardiographic measures (IVC collapsibility index and LVOT VTI

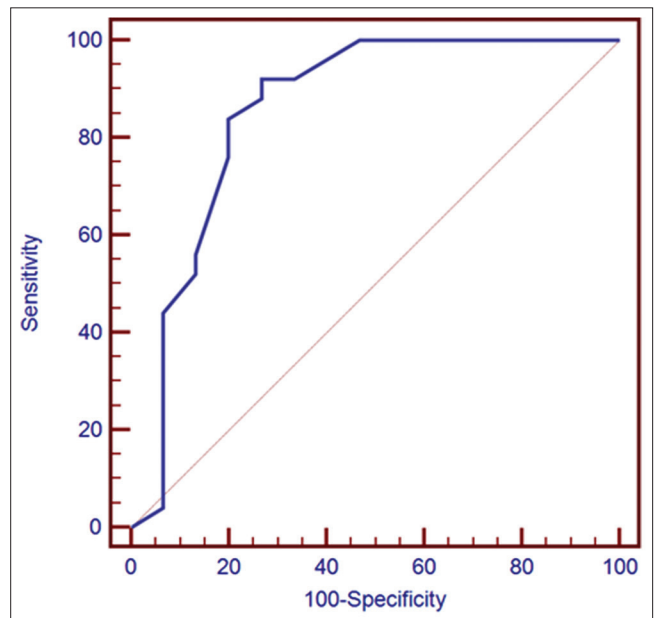


Figure 2: Sensitivity and specificity of left ventricular outflow tract velocity time integral variability index

variability index), both were measured before and after fluid resuscitation.

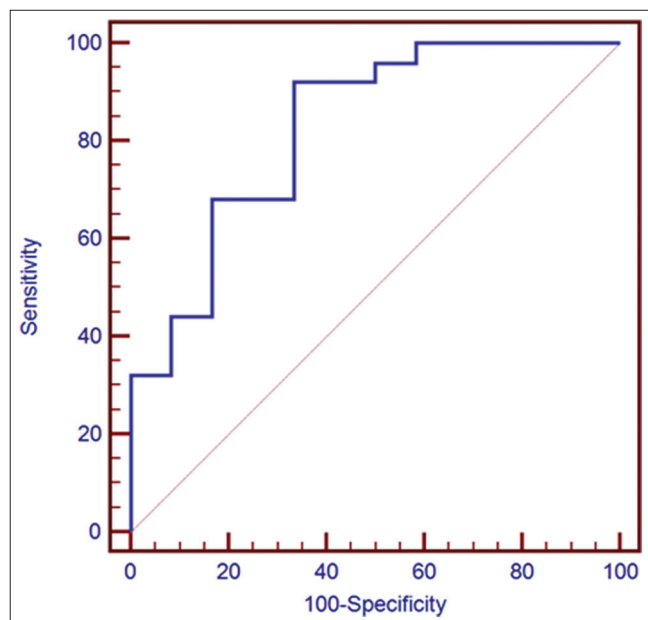


Figure 3: Sensitivity and specificity of cardiac output change

Michard and Teboul, 2002 [13], compared different dynamic and static echocardiographic measures for the prediction of fluid responsiveness in 334 ICU shocked patients and concluded that dynamic measures mainly IVC collapsibility index and LVOT VTI variability index were more accurate and predictive than

**Table 4: Sensitivity and specificity of echocardiographic measures of the studied groups**

Parameter	AUC	Cutoff point	Sensitivity	Specificity	PPV	NPV
IVC collapsibility index	0.995	>18	100.0	93.33	96.2	100.0
LVOT VTI variability index	0.857	>20.5	92.0	73.33	85.2	84.6
CO increase	0.827	>5.66	92.00	66.67	85.2	80.0

CO: Cardiac output; LVOT VTI: Left ventricular outflow tract velocity time integral; IVC: Inferior vena cava.

static measures. The same was concluded by Huggins *et al.*, 2015 [11], and Miller and Mandeville, 2016 [14]. The latter study found that LVOT VTI variability index and IVC collapsibility index through respiratory cycle of  $\geq 12\%$  predict fluid responsiveness. Furthermore,

**Table 5: Central venous line insertion**

CVL	All patients (%)	Group 1 no.=75 (%)	Group 2 no.=45 (%)	Test value	p-value
-ve	87 (72.5)	72 (96.0)	15 (33.3)	55.398*	0.0000
+ve	33 (27.5)	3 (4.0)	30 (66.7)		

CVL: Central venous line

Coen *et al.*, 2014 [15], studied fluid responsiveness in 47 patients with septic shock, using IVC collapsibility index and confirmed that IVC collapsibility index is good predictor of fluid responsiveness. Moreover, the study of Zhao and Wang, 2016 [16], on 42 septic patients concluded that IVC collapsibility index  $< 15\%$  indicates

**Table 6: In-hospital mortality of the studied groups**

In-hospital mortality	Group 1 No. (%)	Group 2 No. (%)	Test value	p-value
Survive	69 (92.0)	18 (40.0)	38.144	0.000
Mortality	6 (8.0)	27 (60.0)		

fluid unresponsiveness. Another 438 patients study provided similar conclusions [17].

The use of echocardiography allowed us to avoid unduly use of central venous catheter in 72.5% of the cases and hence its complications, especially in these patients with high bleeding tendency. This result matches with Coen *et al.*, 2014 [15], who studied 47 patients with septic shock, used the variability of IVC diameter to decide the volume responsiveness, and found that central venous catheter was avoided in more than one-third of the patients.

Furthermore, De Lorenzo *et al.* [18] who carried out a prospective study on 72 patients to investigate volume responsiveness by bedside assessment of IVC and its relation with CVP, they concluded that the subxiphoid ultrasonography IVC assessment is the most reliably correlated with CVP aiming to avoid unduly use of central venous catheter.

Huggins *et al.*, 2016 [11], in a case study, demonstrated that the use of echocardiography improves assessment of volume status in cirrhosis and HRS using IVC collapsibility index and LVOT VTI variability index.

## Conclusions

The use of echocardiography is a good tool for hemodynamic monitoring of fluid resuscitation in cirrhotic patients with AKI. It limited the use of CVL to patients with hemodynamic instability who needed vasoactive support.

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