Can Ultrasonographically Inferior Vena Cava Measured Parameters Guide Fluid Management and Improve the Prognosis AND Renal Outcome IN Patients with Acute Kidney Injury IN Intensive Care Unit?

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Abstract:

Background: It is clear that AKI is a major ICU syndrome with an incidence of some degree of renal dysfunction being reported in greater than 50%. Objective: In patients with AKI, if fluid therapy guided with IVC dimensions, as assessed by bedside ultrasound can be associated with improved renal function and outcome compared to fluid therapy guided with CVP. Patients and methods: A prospective single blinded randomized observational cohort study (Prospective observational study) was carried out on forty (40) patients with AKI during 24 months who admitted to ICU at Ain Shams University Hospitals, Cairo, Egypt. Full history taking, clinical examination, Ultrasonography, and Fluid balances were studied for each patent included in this study. In this study, 40 ICU patients with AKI - according to (KDIGO 2012) criteria - was included and divided into groups 1 and 2, each group included 20 patients matched as regard age, BMI and sex. Patient in group 1 was managed with fluid challenge in concordance with their IVC – CI > 50% in spontaneously breathing patients and in mechanically ventilated patients with a Δ IVC > 12% and then each patient was received 250 ml normal saline infusion as fluid challenge and repeated every 4 hours with repeated IVC diameter measurement. In group 2, patients were managed also with fluid challenge in concordance with their CVP; where a CVP of 8 – 12 cm H2O was considered a target and CVP less than 8 cm H2O an indicator for fluid challenge, and each patient was received 250 ml normal saline infusion as fluid challenge and repeated every 4 hours with repeated CVP diameter measurement also. Both group also followed by repeated serum creatinine and renal urine output every 8 hours too. Results: In group 1 the mean of IVC collapsibility at the start point was 59.75 + 4.58% and after the first 24 hours was 34.8 + 4.99% and after 48 hours was 26.85 + 1.35% while in patients on mechanical ventilator the first Δ IVC at the start point was 51.55 + 3.68% and after 24 hours was 27.55 + 139% and after 48 hours was 17.15 + 1.57%. and in group 2 the mean of CVP at the start of study was 4.3 + 3.37 cm H2O and after 24 hours with fluid therapy was 7.2 + 1.77 cm H2O and after 48 hours was 11.15 + 1.46 cm H2O. At the start point of this study, the mean of patient's creatinine were 2.78 + 0.39 mg/dl in group 1 and were 2.93 + 0.51 mg/dl in group 2 and after 24 hours of fluid therapy challenge, the mean of serum creatinine in group 1 were 1.95 + 0.32 mg/dl and in group 2 were 1.94 + 0.51 mg/dl, and after 48 hours the mean of serum creatinine in group 1 were 1.15 + 0.28 mg/dl and in group 2 were 1.2 + 0.33 mg/dl. Also, in group 1 the mean of urine output rate at zero time after diagnosis and before fluid therapy were0.46 + 0.25 ml/kg/h and in group 2 were 0.51 + 0.36 ml/kg/h and after 24 hours, the mean of urine output were 0.6 + 0.34 ml/kg/h in group 1 and were 0,57 + 0.49 ml/kg/h and after 48 hours were 1.53 + 0.22 ml/kg/h in group 1 and were 1.74 + 0.68 ml/kg/h in group 2. In conclusion, in patients with AKI, the only indication for fluid administration is correction or prevention of intravascular hypovolemia. If fluids are considered to be necessary, boluses of small aliquots should be considered instead of rapid high volume fluid administration. Follow up of correction of hypovolemia in such state can be effective by measuring IVC diameter by Ultrasound or by measuring CVP; both are good and kidney function outcome also is improved.

Keywords: Inferior Vena Cava, Acute Kidney Injury, Intensive Care Unit

1. Introduction

Acute kidney injury (AKI), a sudden and sustained decline in renal function, is a frequent and devastating clinical problem and its incidence has increased markedly (1). In hypovolemia, inadequate fluid resuscitation results in tissue hypoperfusion and worsening end- organ dysfunction, and resuscitation strategies that avoid under resuscitation have a proven mortality benefit (2). Pre-renal form of AKI is by far the most common in the ICU and is considered, at least in its initial phases, to be

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functional in nature (i.e. there are no histopathological changes to renal tissue). The term indicates that the kidney malfunctions predominantly because of systemic factors outside the kidney, which decrease GFR (decreased cardiac output, hypotension, sepsis and the like). If the systemic cause of AKI is rapidly removed or corrected, renal function improves and relatively rapidly returns to near normal levels (3). Intravascular volume must be maintained or rapidly restored, and this is often best done using invasive hemodynamic monitoring (central venous catheter, arterial cannula, and pulmonary artery catheter or pulse contour cardiac output catheters) (4).

Sonographic evaluation of the IVC diameter and its usefulness in evaluating the volume status are studied and documented. Bedside ultrasonography is readily available in intensive care setups. It is safe, cheap and non-invasive. ultrasound of inferior vena cava (IVC) is a tool that can provide a rapid and non-invasive means of gauging preload and the need for fluid resuscitation (5, 6). These Changes in volume status is detected in ultrasonographic evaluation of the IVC, where increased or decreased collapsibility of the vessel will help clinicians and intensivists in guiding clinical management of the patient (7). Bedside sonography measuring the inferior vena cava diameter and collapsibility index to determine volume status is a relatively new, promising area of research for identifying individuals at risk of dehydration (8).

So, the aim of the study is to investigate patients with AKI, if fluid therapy guided with IVC dimensions, as assessed by bedside ultrasound can be associated with improved renal function and outcome compared to fluid therapy guided with CVP.

2. Patients and Methods

Type of study

Prospective single-blinded randomized observational cohort study (Prospective observational study)

Study Setting

The study was carried out at Ain Shams University Hospitals, Cairo, Egypt. This study was approved by the ethical committee of Ain Shams School of Medicine, and all patients gave a written informed consent for participation.

Study Period: 24 months between

Study population

All patients who were admitted to ICU at Ain Shams University Hospitals with a diagnosis of AKI (defined by a rise in serum creatinine level from baseline of at least 0.3 mg/dL within 48 h or at least 50% higher than baseline or reduction in urine output to less than 0.5 mL/kg/h for longer than 6 h (Ostermann, 2012).

Exclusion criteria:

1. Patients who received more than 2 L of fluids before enrolment in this study.
2. Age <18 years.
3. Chronic hemodialysis or ongoing continuous renal replacement therapy (CRRT).
4. Obstructive uropathy.
5. Pulmonary emboli.
6. Clinical signs of elevated abdominal pressure.
7. Moderate to severe tricuspid regurgitation.
8. Absence of informed consent.

Sample size:

Using the PASS program for sample size calculator and according to Jambieh and coworkers (2017), the expected proportion with improved creatinine in group 1 = 85% and in group 2 = 31% sample size of 20 patients in each group can detect this difference with power 97% and x- error 0.05.

Population and study settings:

Forty patients were randomly divided into two groups:

Group 1: included 20 patients who were managed in concordance with their IVC measurements, where spontaneously breathing patients with an IVC-CI ≥50% and mechanically ventilated patients with a ΔIVC ≥12% received 250 ml of normal saline with repeated IVC diameter measurement every 4 h plus measurement of hemodynamic parameters including heart rate, blood pressure, and urine output, for 48 hours after admission.

A two-dimensional echocardiographic sector was used to visualize the long axis of the IVC at the subcostal window. The M-mode was used to generate a time-motion record of the IVC diameter approximately 2cm caudal to its junction with the right atrium. The maximum (IVC max) and minimum (IVC min) diameters of the IVC over a single respiratory cycle were collected. One critical care physician completed the ultrasound examination of the IVC diameter of all enrolled eligible patients.

In spontaneously breathing non-ventilated patients, the IVC-CI was calculated as:

(IVCmax − IVCmin)/IVCmax.

In mechanically ventilated patients, we calculated the ΔIVC as:

(IVCmax − IVCmin)/[0.5 × (IVCmax + IVCmin)]

while the patient was breathing comfortably, without any significant patient-ventilator asynchrony, and using a tidal volume of 8–10 ml/kg of ideal body weight (Feissel et al., 2004). We used the IVC-CI (≥50%) and ΔIVC (≥12%) to classify patients as potential candidates for fluid administration in spontaneously breathing and mechanically ventilated patients, respectively.

M. Feissel, F. Michard, J.-P. Faller, and J.-L. Teboul (2004). "The respiratory variation in inferior vena cava diameter as a guide to fluid therapy," Intensive Care Medicine; 30 (9): 1834– 1837.

Group 2: included 20 patients in whom CVP was used to guide fluid challenges, where a CVP of 8–12 cm H2O was considered a target; a CVP less than 8 cm H2O the patient was considered hypovolemic and candidate for a fluid challenge and each patient received 250 ml of normal saline; and patients having CVP >12 cm H2O were considered as hypervolemic; with repeated CVP measurements every 4 h plus measurement of hemodynamic parameters including

heart rate, blood pressure, and urine output, for 48 hours after admission.

The CVP was uniformly measured from a recording at end-expiration with the patient supine and the CVP manometer having been zeroed at the mid-thoracic position.

Each patient in this study was subjected to:

Thorough medical history taking and physical examination.

The baseline clinical characteristics of all patients were collected including age, sex, past medical history, primary admission diagnosis, hemodynamic parameters, laboratory parameters, and echocardiographic parameters. Baseline, day 0 (inclusion day), and day 2 data were collected for all participants. Fluid balances as well as the plasma creatinine level at 48 hours after admission were recorded.

The management of the patients was done by the primary intensive care team without knowledge of the results of the ultrasound measurements.

The primary outcome was defined as the percentage of patients with improved creatinine levels at 48 hours in both groups.

Secondary outcomes included fluid challenges and changes in serum creatinine and urine output.

If patients were started on hemodialysis or CRRT, we considered them as if their creatinine did not improve and they were excluded from the final analysis.

Statistical analysis

Data are presented as means ± standard deviation and percentages.

Two types of statistics were done:

i. Descriptive statistics: e.g. percentage **(%)**, mean **(X)**, and standard deviation **(SD)**.

ii. Analytic statistics: e.g. Chi-square test, F-test **(ANOVA-analysis of variance)**:

1. Chi-square test: a test of significance used for comparison between two groups having qualitative variables.
2. F-test (ANOVA - analysis of variance): is a test of significance used for comparison between more than two groups having quantitative variables.
3. t-test: a test of significance used for comparison between two groups having quantitative variables with different variances (parametric test).
4. Z-test: a test of significance used for comparison between two means.
5. P value of <0.05 was considered to be statistically significant, whereas P value <0.001 was considered highly significant, on the other hand P value >0.05 was considered statistically not significant.

3. Results

1. This study was conducted at Ain Shams University Hospital ICUs. A total of 55 patients were enrolled and consented to participate in the study. Fifteen patients were excluded from the final analysis as follows:
2. Three patients in group 1 developed irreversible shock and died following recruitment.
3. Another seven patients in group 1 did not respond to fluid challenges and required renal replacement therapy.
4. Five patients in group 2 were excluded not responding to fluid challenges and required renal replacement therapy.
5. The remaining patients were classified into 2 groups 20 patients in each group (Figure 4).

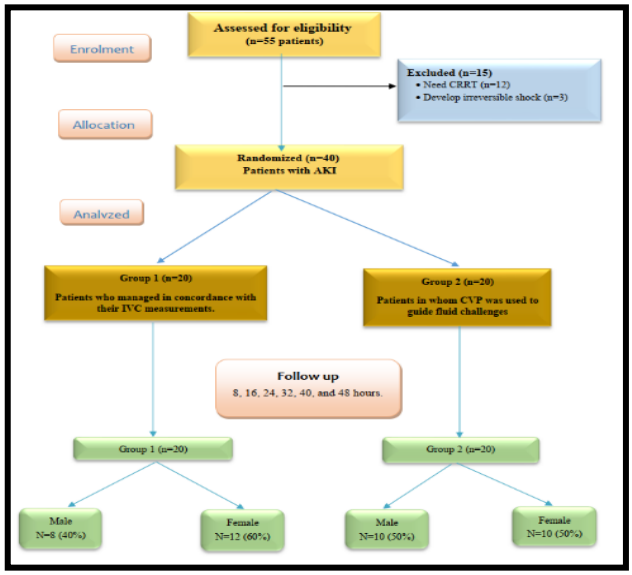

Figure (1): Flowchart of the recruited patients

Table (1): Clinical characteristics				
	Group 1 N=20	Group 2 N=20	P value	Level of significance
Age (years)				
Mean ± SD	54.2 ± 4.58	54.05 ± 5.16	0.9732	NS
Minimum	47	45		
Maximum	62	61		
BMI (kg/m2)				
Mean ± SD	29.95 ± 5.38	31.15 ± 5.16	0.464	NS
Sex				
Male (%)	8 (40)	10 (50)	0.7506	NS
Female (%)	12 (60)	10 (50)		
Statistical test used: Two sample t-test & Chi-Square Test p-value ≤0.05 considered statistically significant (95% confidence interval).				

The baseline characteristics of these patients are summarized in Tables 1, 2, and 3. A total of 22/40 (55%) females and 18/40 (45%) males were included in the study with a mean age of 52.2 ± 19.3 years.

There was no significant difference in the baseline characteristics of both groups including age, sex, body mass index (Table 1), medical history, medical comorbidities (Table 2), primary admission, and final diagnosis (Table 3).

Table (2): Original comorbidities				
	Group 1 N=20	Group 2 N=20	P value	Level of significance
Hypertension				
Positive (%)	15 (75)	9 (45)	0.1066	NS
Diabetes mellitus				
Positive (%)	11 (55)	13 (65)	0.7469	NS
Statistical test used: Two sample Chi-Square Test p-value ≤0.05 considered statistically significant (95% confidence interval).				

Table (3): Primary admission and final diagnosis				
	Group 1 N=20	Group 2 N=20	*P* value	Level of significance
Final diagnosis				
Sepsis				
Positive (%)	8 (40)	12 (60)	0.3428	NS
Pneumonia				
Positive (%)	9 (45)	9 (45)	0.7506	NS
Congestive heart failure				
Positive (%)	3 (15)	2 (10)	0.632	NS
Myocardial infarction				
Positive (%)	5 (25)	5 (25)	1.000	NS
Diabetic ketoacidosis/Hyperglycemic hyperosmolar				
Positive (%)	6 (30)	9 (45)	0.5136	NS
GI bleeding				
Positive (%)	8 (40)	12 (60)	0.3428	NS
Hepatic encephalopathy				
Positive (%)	4 (20)	6 (30)	0.465	NS
Statistical test used: Chi-Square Test p-value ≤0.05 considered statistically significant (95% confidence interval).				

Table (4): Hemodynamic data analysis				
	Group 1 N=20	Group 2 N=20	P value	Level of significance
Hemodynamic				
Mean arterial pressure (mmHg)	82.3 ± 7.91	83.75 ± 7.72	0.5242	NS
Heart rate (bpm)	102.85 ± 9.69	93.9 ± 8.46	0.0031	Significant
Vasopressors required				
Positive (%)	11 (55)	8 (40)	0.5266	NS
Baseline ejection fraction (%)	62.15 ± 3.76	61.05 ± 4.74	0.4722	NS
Statistical test used: Two sample t-test & Chi-Square Test p-value ≤0.05 considered statistically significant (95% confidence interval).				

The mean heart rate was significantly lower in group 2 (p = 0.03), although the other hemodynamic variables including the number of patients on vasopressors were not statistically different between both groups **(Table 4)**.

Table (5): Laboratory data analysis				
	Group 1 N=20	Group 2 N=20	P value	Level of significance
Blood Data				
Na (mmol/L)	136.1 ± 2.85	134.75 ± 3.16	0.1869	NS
Albumin (g/dL)	2.44 ± 0.33	2.55 ± 0.35	0.3359	NS
BNP (pg/mL)	229.15 ± 100.84	224.8 ± 129.26	0.862	NS
Statistical test used: Two sample t-test p-value ≤0.05 considered statistically significant (95% confidence interval).				

There was no statistically significant difference in the laboratory investigations of both groups **(Table 5)**.

Table (6): Ultrasound data analysis				
	Group 1 N=20	Test value	P-value	Level of significance
IVC-CI	Mean ± SD			
Baseline	59.75 ± 4.58	–	–	–
4 hrs	54.25 ± 2.86	6.080	< 0.001	HS
8 hrs	48.2 ± 5.11	6.449	< 0.001	HS
12 hrs	44.50 ± 2.89	11.487	< 0.001	HS
16 hrs	40.3 ± 3.13	16.644	< 0.001	HS
20 hrs	37.70 ± 1.95	22.439	< 0.001	HS
24 hrs	35.8 ± 3.19	23.483	< 0.001	HS
28 hrs	32.80 ± 2.28	23.807	< 0.001	HS
32 hrs	30.4 ± 4.99	18.253	< 0.001	HS
36 hrs	29.20 ± 2.73	25.235	< 0.001	HS
40 hrs	27.65 ± 1.79	31.140	< 0.001	HS
44 hrs	27.50 ± 1.00	32.694	< 0.001	HS
48 hrs	23.85 ± 1.35	31.995	< 0.001	HS
ΔIVC	Mean ± SD			
Baseline	15.80 ± 2.61	–	–	–
4 hrs	15.20 ± 2.38	3.040	0.007	HS
8 hrs	14.70 ± 2.05	3.488	0.002	HS
12 hrs	14.30 ± 1.95	4.459	< 0.001	HS
16 hrs	13.65 ± 1.95	6.015	< 0.001	HS
20 hrs	13.25 ± 2.07	6.706	< 0.001	HS
24 hrs	12.70 ± 1.89	7.233	< 0.001	HS
28 hrs	12.15 ± 2.01	7.167	< 0.001	HS
32 hrs	11.65 ± 1.84	8.409	< 0.001	HS
36 hrs	11.30 ± 1.95	8.252	< 0.001	HS
40 hrs	10.85 ± 1.98	9.161	< 0.001	HS
44 hrs	10.10 ± 1.62	10.052	< 0.001	HS
48 hrs	9.55 ± 1.39	10.865	< 0.001	HS
Statistical test used: Two sample *t*-test *p*-value ≤0.05 considered statistically significant (95% confidence interval).				

3).

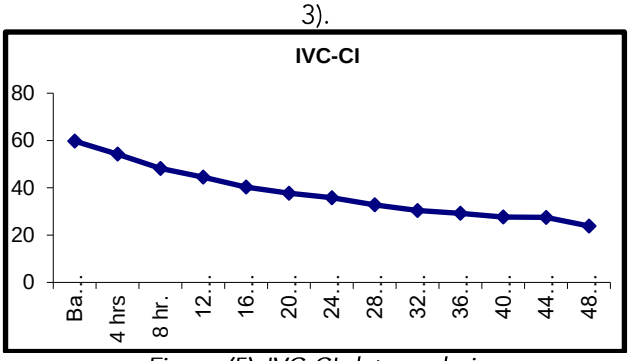

Figure (5): IVC-CI data analysis

In spontaneously breathing patients, the mean baseline IVC-CI index was 59.75 ± 4.58%, and in mechanically ventilated patients the mean baseline ΔIVC was 15.80 ± 2.61in group 1. Compared to the baseline, there was a highly significant improvement in both indices all through the study period in group 1 (Table 6) (Figures 5 & 6).

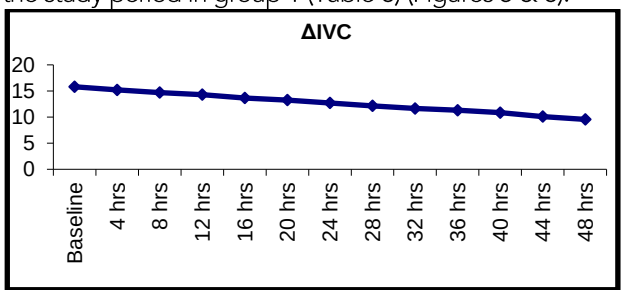

Figure (6): ΔIVC data analysis

Table (7): CVP data analysis				
	Group 2 N=20	Test value	P-value	Level of significance
CVP (cm H2O)	Mean ± SD			
Baseline	4.3 ± 3.37	–	–	–
4 hrs	6.15 ± 1.84	-4.122	0.001	HS
8 hrs	7.65 ± 1.6	-3.941	0.001	HS
12 hrs	7.80 ± 1.51	-4.129	0.001	HS
16 hrs	7.4 ± 1.82	-3.721	0.001	HS
20 hrs	7.55 ± 1.19	-4.092	0.001	HS
24 hrs	7.2 ± 1.77	-3.298	0.004	HS
28 hrs	7.65 ± 1.39	-4.193	< 0.001	HS
32 hrs	7.6 ± 1.88	-4.134	0.001	HS
36 hrs	8.20 ± 1.11	-5.378	< 0.001	HS
40 hrs	8.1 ± 1.52	-5.026	< 0.001	HS
44 hrs	9.90 ± 1.21	-7.519	< 0.001	HS
48 hrs	11.15 ± 1.46	-8.872	< 0.001	HS
Statistical test used: Two sample t-test p-value ≤0.05 considered statistically significant (95% confidence interval).				

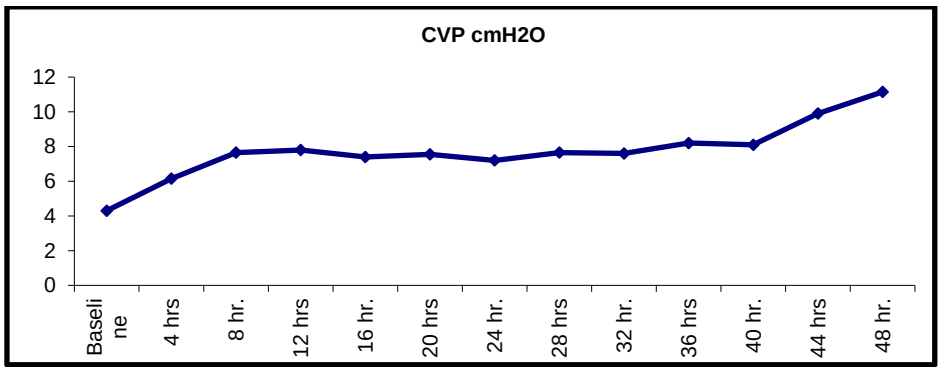

Figure (7): CVP data analysis

The mean central venous pressure at baseline was 4.3 ± 3.37 cmH2O in group 2. Compared to the baseline, there was a highly significant improvement in the mean central venous pressure all through the study period in group 2 (Table 7) (Figure 7).

Table (8): Mean serum creatinine data analysis				
	Group 1 N=20	Group 2 N=20	P value	Level of significance
Creatinine (mg/dL)				
Baseline	2.78 ± 0.39	2.93 ± 0.51	0.5073	NS
12 hrs	2.15 ± 0.38	2.09 ± 0.53	0.5876	NS
24 hrs	1.95 ± 0.32	1.94 ± 0.49	0.6538	NS
36 hrs	1.49 ± 0.27	1.49 ± 0.34	0.984	NS
48 hrs	1.15 ± 0.28	1.2 ± 0.33	0.3723	NS
Statistical test used: Two sample t-test p-value ≤0.05 considered statistically significant (95% confidence interval).				

Serum creatinine improved in both groups compared to baseline levels with no statistically significant differences between both groups all through the study period (Table 8) and (Figure 8).

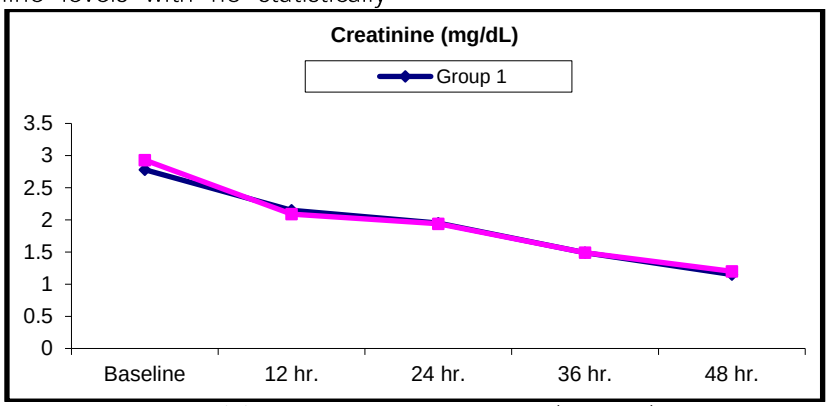

Figure (8): Mean serum creatinine data analysis

Table (9): Urine output data analysis				
	Group 1 N=20	Group 2 N=20	*P* value	Level of significance
Urine output ml/kg/h				
Baseline	0.46 ± 0.25	0.51 ± 0.36	0.6346	NS
4 hrs	0.44 ± 0.14	0.43 ± 0.24	0.850	NS
8 hrs	0.41 ± 0.23	0.34 ± 0.27	0.2617	NS
12 hrs	0.44 ± 0.18	0.50 ± 0.30	0.492	NS
16 hrs	0.47 ± 0.23	0.65 ± 0.54	0.6442	NS
20 hrs	0.54 ± 0.15	0.61 ± 0.34	0.367	NS
24 hrs	0.6 ± 0.34	0.57 ± 0.49	0.4489	NS
28 hrs	0.64 ± 0.23	0.74 ± 0.43	0.396	NS
32 hrs	0.68 ± 0.36	0.9 ± 0.76	0.9307	NS
36 hrs	1.13 ± 0.24	0.94 ± 0.44	0.093	NS
40 hrs	1.57 ± 0.32	0.98 ± 0.64	0.0014	Significant
44 hrs	1.55 ± 0.20	1.36 ± 0.46	0.091	NS
48 hrs	1.53 ± 0.22	1.74 ± 0.68	0.1759	NS
Statistical test used: Two sample *t*-test *p*-value ≤0.05 considered statistically significant (95% confidence interval).				

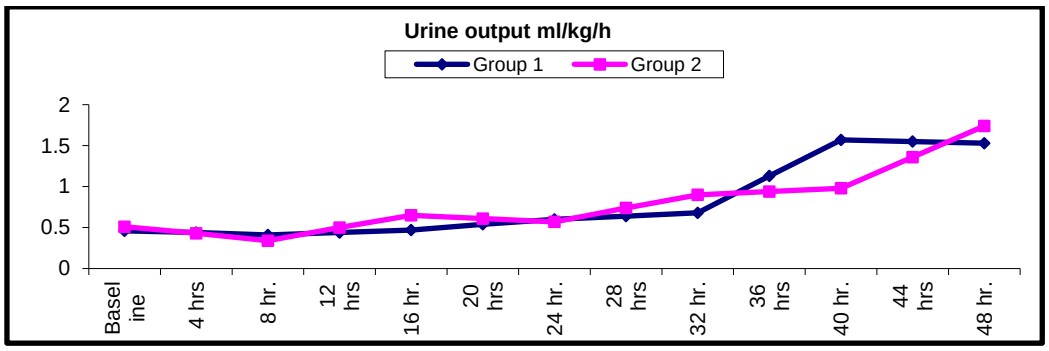

Figure (9): Urine output data analysis

Compared to baseline levels, there was a significant improvement in the renal function in both groups as evidenced in the volume of UOP with no statistically significant differences between both groups all through the study period (Table 9) and (Figure 9).

Table (10): Fluid challenges data analysis					
Fluid challenges	Group I No. = 20	Group II No. = 20	Test value	*P*-value	Level of significance
Baseline	250.00 ± 0.00	250.00 ± 0.00	–	–	–
4 hrs	192.50 ± 40.64	190.00 ± 34.79	0.209•	0.836	NS
8 hrs	200.00 ± 36.27	192.50 ± 46.67	0.567•	0.574	NS
12 hrs	192.50 ± 40.64	205.00 ± 45.60	-0.915•	0.366	NS
16 hrs	192.50 ± 43.75	200.00 ± 28.10	-0.645•	0.523	NS
20 hrs	207.50 ± 40.64	192.50 ± 33.54	1.273•	0.211	NS
24 hrs	185.00 ± 23.51	172.50 ± 34.32	1.344•	0.187	NS
28 hrs	187.50 ± 39.32	195.00 ± 35.91	-0.630•	0.533	NS
32 hrs	192.50 ± 33.54	192.50 ± 46.67	0.000•	1.000	NS
36 hrs	205.00 ± 42.61	207.50 ± 46.67	-0.177•	0.861	NS
40 hrs	197.50 ± 44.35	197.50 ± 30.24	0.000•	1.000	NS
44 hrs	202.50 ± 44.35	182.50 ± 29.36	1.682•	0.101	NS
48 hrs	180.00 ± 29.91	172.50 ± 34.32	0.737•	0.466	NS

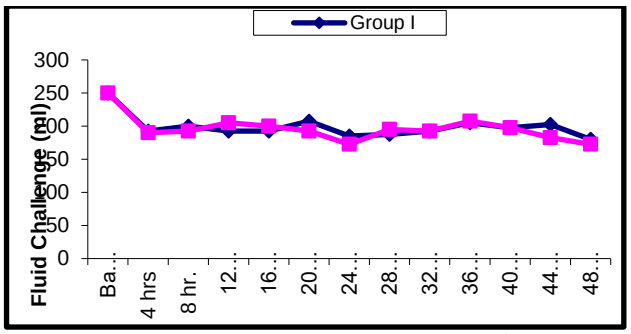

Figure (10): Fluid challenge data analysis for study groups

The mean normal saline volumes given as fluid challenges were compared between both groups. All patients received 250 mL of normal saline at the start of the trial. Later on, there was no statistically significant difference between both groups in the volume of fluid challenges given to all patients throughout the study period (Table 10) and (Figure 10).

A Pearson correlation was run to determine the relationship between the central venous pressure values, the inferior vena cava collapsibility indices (IVC-CI%) and the inferior vena cava variation indices (ΔIVC) with the improvement in serum creatinine and urine output in both groups (Tables 11 & 12). No significant correlation was observed between the central venous pressure values, IVC-CI%, and ΔIVC with the improvement in serum creatinine and urine output in both groups.

Table (11): Correlation between IVC-CI, and ΔIVC with creatinine and urine output				
Group I	% evolution of IVC-CI		% evolution of ΔIVC	
	r	*P*-value	r	*P*-value
% improvement of Creatinine	0.222	0.347	0.081	0.736
% improvement of UOP	-0.013	0.957	-0.126	0.597

Table (12): Correlation between CVP values with creatinine and urine output		
Group II	% increase of CVP	
	r	*P*-value
% improvement of Creatinine	-0.259	0.316
% improvement of UOP	-0.016	0.951

4. Discussion

In our study, guided fluid therapy in critically ill patients with AKI based on the use of bedside ultrasound to assess IVC variation and collapsibility indices or by measurement of CVP was associated with improved renal function at 48 hours. However, there was no linear correlation between the CVP and

IVC variation and collapsibility indices with improved renal function.

AKI is a common diagnosis in the ICU, involving 13% to 78% of admissions. Accurate assessment of the fluid status is essential to its management. Its pathophysiology involves multiple mechanisms, including hypovolemia and various types of shock. Although fluid loading can be helpful by restoring the renal perfusion pressure in many hypovolemic patients with pre-renal failure, it may be deleterious in hypervolemic patients with renal hypoperfusion related to a low cardiac output, where further fluid loading can lead to pulmonary edema and deterioration in oxygenation (Brochard et al., 2010). Moreover, fluid overload in ICU patients has been shown to be an independent risk factor for the development of AKI, as well as the 28-day mortality in these patients (Wang et al., 2015).

Fluid administration is also imperative for preventing AKI associated with circulatory failure. Maintaining a correct mean arterial pressure (MAP) has long been regarded as the primary goal in preventing AKI, especially in vasopressor-dependent patients. However, MAP does not reflect changes in renal hemodynamics that determine renal perfusion. Low diastolic arterial pressure, decreased mean perfusion pressure, and high CVP were associated with AKI in septic and post-cardiac surgery patients whereas a MAP deficit was not (Wong et al., 2015; Honoré et al., 2019).

In a broad spectrum of patients with and without reduced cardiac function, a significant association between increased CVP and impaired renal function has been recognized. Increasing evidence points to a close relationship between venous congestion, as estimated by CVP, and AKI. Elevated CVP is independently correlated with prolonged treatment and poor outcomes in critical care settings (Li et al., 2017; Chen et al., 2018).

Venous congestion, rather than reduced cardiac output, may be the primary hemodynamic factor driving worsening renal function in patients with acute and chronic heart failure (Uthoff et al., 2011).

Fluids should only be administered until intravascular hypovolemia has been corrected. It is desirable to administer the minimum amount of intravenous fluid required to maintain perfusion and systemic oxygen delivery. If fluids are considered necessary, they should be administered in frequent small aliquots and under periodic reassessment of fluid responsiveness and hemodynamic status so that fluid overload is avoided (Ostermann et al., 2019).

Accurate prediction of fluid responsiveness allows rational fluid resuscitation while avoiding the consequences of an excess fluid challenge; these consequences may include excess tissue and pulmonary edema with a deleterious impact on respiratory function, wound healing, and abdominal compartment syndrome (Sturgess and Watts, 2019).

Functional hemodynamic monitoring builds upon the observation that 'dynamic' hemodynamic variables are better predictors of response to fluid challenge than 'static' variables (Michard et al., 2020).

The CVP is determined by the interaction between cardiac function and venous return, which in turn are influenced by total blood volume, vascular tone, cardiac output, right ventricular compliance, and intrathoracic, abdominal, and pericardial pressures (Gelman, 2008).

When correctly measured, CVP reflects the right atrial pressure and volume status of the right and, to a lesser extent, the left ventricle. In critically ill patients, CVP is used to assess cardiac preload and volume status and to assist in the diagnosis of right- and left-sided heart failure (Magder, 2017).

Measuring CVP is still considered to be useful for guiding fluid resuscitation in critically ill patients, especially when followed over time and in combination with cardiac output recording (De Backer & Vincent, 2018).

Recent international guidelines have recommended that the use of CVP alone to guide fluid resuscitation can no longer be justified. According to these guidelines, volume status and tissue perfusion may be assessed by focused examination, or a combination of two of CVP, central venous oxygen saturation, cardiovascular ultrasound and other dynamic measures like the passive leg raise or fluid challenge. CVP catheter insertion is invasive and time-consuming (Rhodes et al., 2016).

Except at extreme values, static measures of CVP do not differentiate patients likely to respond to fluid therapy from non-responders. Traditionally, dynamic changes in CVP, either in response to volume loading or related to respiration, have been used to assist in evaluating volume status, but these principles may be misapplied. A steep increase in CVP following volume challenges may suggest that the heart is functioning on the plateau portion of the Frank-Starling curve. Severe hypotension with a low or normal CVP is unlikely to be solely due to acute pulmonary embolism, cardiac tamponade, or tension pneumothorax (Magder, 2015).

It must also be appreciated that the majority of 'dynamic' variables posed as predictors of fluid responsiveness have been studied in small samples of highly selected patients under restrictive preconditions (including mandatory mechanical ventilation). In particular, techniques such as pulse pressure variation have been validated only under a number of caveats including the absence of spontaneous respiratory effort, moderate tidal volumes, and normal myocardial contractility. Assessing the response to a fluid challenge or passive leg rising is more generalizable and is more commonly recommended (Teboul et al., 2019).

Early interest in the role of IVC-US in the determination of intravascular volume status focused on correlating IVC diameter (size) with measured CVP. The results of these initial studies suggested that mean IVC diameter correlated with CVP. More recent work, however, has demonstrated a more modest correlation between IVC diameter with

CVP (Stone et al., 2013).

A useful and simple method of assessing intravascular volume is by IVC diameter and collapsibility. The collapsibility index is associated with volume status. It was found to be significantly higher in patients with volume loss (Fields et al., 2011).

Feissel and associates (2004) used the IVC-CI (≥50%) and ΔIVC (≥12%) to classify patients as potential candidates for fluid administration in spontaneously breathing and mechanically ventilated patients, respectively. Intravascular volume depletion is likely when the IVC-CI is >50%. In mechanically ventilated patients, the IVC Variation Index (ΔIVC) correlates with volume responsiveness, and volume responsiveness is likely when the ΔIVC is ≥12% in these patients.

Patients with small IVCs and increased collapsibility should benefit from volume expansion. Patients with increased IVC diameters and decreased collapsibility may be volume overloaded and need a reassessment of their clinical status and more cautious fluid challenge trials (Yepes-Hurtado, et al., 2016).

There is a reasonably good correlation between IVC dimension measurements and CVP measurements. There was a good correlation between volume responsiveness defined as an increase in cardiac index ≥15% and the presence of a baseline distensibility index of 18%. These results suggest that the measurement of inferior vena cava in critically ill patients can facilitate decisions regarding fluid management (Barbier et al., 2004).

The IVC collapsibility increased significantly after ultrafiltration, and hypotension occurred only in patients who had an IVC collapsibility index greater than 30%. These results suggest that IVC measurements can help determine the volume status in patients with chronic cardiac failure (Guiotto et al., 2010).

Sobczyk and his colleagues (2015) studied IVC measurements during the first 6 hours in patients who had just completed cardiac surgery. They found a weak correlation between central venous pressures and IVC-derived parameters. In addition, they found no statistically significant differences between patients who were fluid responders and patients who were non-responders in IVC measurements or IVC-derived indices.

De Lorenzo and co-workers (2012) conducted a prospective study on 72 patients to investigate volume responsiveness by bedside assessment of IVC and its relation with CVP, and concluded that the subxiphoid ultrasonography IVC assessment is the most reliably correlated with CVP aiming to avoid unduly use of the central venous catheter.

In patients with spontaneous ventilation, respiratory variations are highly variable. An IVC-CI ≥50% has been shown to strongly correlate with hypovolemia and low CVP in critically ill spontaneously breathing patients (Thanakitcharu et al., 2013).

Thanakitcharu P, Charoenwut M, Siriwiwatanakul N: Inferior vena cava diameter and collapsibility index: a practical non-invasive evaluation of intravascular fluid volume in critically-ill patients. J Med Assoc Thai. 2013; 96: S14-22.

In critically ill patients with AKI, the concurrence of fluid therapy with IVC predicted fluid management, as assessed by bedside ultrasound, was associated with improved renal function at 48 hours (Jambeih et al., 2017).

Ilyas and associates (2017) demonstrated a positive relationship between CVP with minimum and maximum IVC diameters but an inverse relation with the IVC collapsibility index. A very high CI (often associated with a very low CVP) may serve as a possible explanation for the beneficial use of giving more fluid without volume overload. As the CI decreases with fluid administration, it becomes increasingly less reliable as a surrogate for intravascular volume.

Ilyas A, Ishtiaq W, Assad S, et al. Correlation of IVC Diameter and Collapsibility Index with Central Venous Pressure in the Assessment of Intravascular Volume in Critically Ill Patients. Cureus 2017;9(2): e1025.

El Hadidy and his colleagues (2020) demonstrated that the IVC collapsibility index showed good predictive value of fluid responsiveness and that responders had significantly higher IVC collapsibility index and the use of IVC collapsibility index is a good tool for hemodynamic monitoring of fluid resuscitation in patients with AKI.

The main limitations of our study are related to:

1. Its observational nature.
2. Small sample size.
3. Single-center trial.
4. The lack of correlation between central venous pressure, inferior vena cava variation index, and the inferior vena cava collapsibility index for estimating the volume status.
5. Lack of assessment of fluid balance.

(Bellomo, 2019). (Garg et al., 2016). (Delaney & Finfer, 2019). (Maitland et al., 2011). (Myburgh et al., 2012). (Arslantas et al., 2022). (Yepes-Hurtado et al., 2016). (Monnet et al., 2016). (Zarbock et al., 2014). (Dellinger et al., 2013). (Honoré et al., 2019).

(Govender et al., 2018).

5. Conclusion

In conclusion, in patients with AKI, the only indication for fluid administration is the correction or prevention of intravascular hypovolemia. If fluids are considered to be necessary, boluses of small aliquots should be considered instead of rapid high-volume fluid administration. Follow-up of correction of hypovolemia in such a state can be effective either by measuring IVC indices by Ultrasound or by measuring CVP; both are good.

Further validation research is required to support our preliminary findings and to confirm a correlation between CVP measurement and ultrasound

assessment of the IVC. CVP and IVC ultrasound should be used as clinical adjuncts, and not as stand-alone measures of volume assessment.

6. Summary

It is clear that AKI is a major ICU syndrome with an incidence of some degree of renal dysfunction being reported in greater than 50%.

In patients with AKI, if fluid therapy guided with IVC dimensions, as assessed by bedside ultrasound can be associated with improved renal function and outcome compared to fluid therapy guided with CVP.

In this study, 40 ICU patients with AKI - according to (KDIGO 2012) criteria - was included and divided into groups 1 and 2, each group included 20 patients matched as regard age, BMI and sex.

Patient in group 1 was managed with fluid challenge in concordance with their IVC – CI > 50% in spontaneously breathing patients and in mechanically ventilated patients with a Δ IVC > 12% and then each patient was received 350 ml normal saline infusion as fluid challenge and repeated every 8 hours with repeated IVC diameter measurement.

In group 2, patients were managed also with fluid challenge in concordance with their CVP; where a CVP of 8 – 12 cm H2O was considered a target and CVP less than 8 cm H2O an indicator for fluid challenge, and each patient was received 350 ml normal saline infusion as fluid challenge and repeated every 8 hours with repeated CVP diameter measurement also.

Both group also followed by repeated serum creatinine and renal urine output every 8 hours too.

In group 1 the mean of IVC collapsibility at the start point was 59.75 + 4.58% and after the first 24 hours was 34.8 + 4.99% and after 48 hours was 26.85 + 1.35% while in patients on mechanical ventilator the first Δ IVC at the start point was 51.55 + 3.68% and after 24 hours was 27.55 + 139% and after 48 hours was 17.15 + 1.57%. and in group 2 the mean of CVP at the start of study was 4.3 +3.37 cm H2O and after 24 hours with fluid therapy was 7.2 +1.77 cm H2O and after 48 hours was 11.15 + 1.46 cm H2O.

At the start point of this study, the mean of patients's creatinine were 2.78 + 0.39 mg/dl in group 1 and were 2.93 + 0.51 mg/dl in group 2 and after 24 hours of fluid therapy challenge, the mean of serum creatinine in group 1 were 1.95 + 0.32 mg/dl and in group 2 were 1.94 + 0.51 mg/dl, and after 48 hours the mean of serum creatinine in group 1 were 1.15 + 0.28 mg/dl and in group 2 were 1.2 + 0.33 mg/dl. Also, in group 1 the mean of urine output rate at zero time after diagnosis and before fluid therapy were 0.46 + 0.25 ml/kg/h and in group 2 were 0.51 + 0.36 ml/kg/h and after 24 hours, the mean of urine output were 0.6 + 0.34 ml/kg/h in group 1 and were 0,57 + 0.49 ml/kg/h and after 48 hours were 1.53 + 0.22 ml/kg/h in group 1 and were 1.74 + 0.68 ml/kg/h in group 2.

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