ORIGINAL RESEARCH ARTICLE

INSIGHTS INTO THE USE OF POINT OF CARE ULTRASOUND (POCUS) GUIDED FLUID RESUSCITATION IN ACUTE PANCREATITIS PATIENTS, PRESENTING WITHIN FIRST 72 HOURS OF ONSET OF PAIN

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Abstract

Background

Intravenous fluid resuscitation plays a critical role in the management of early acute pancreatitis. Central venous pressure (CVP) measurement as a guide to estimation of intravascular volume is the standard of care however, Echocardiography in the intensive care unit is an emerging non-invasive alternative for intravascular volume estimation. Many static and dynamic parameters measured by it provide an estimation of fluid responsiveness in such patients, like IVC diameter, pulmonary artery occlusion pressure using Doppler indices, right and left ventricular diameter and changes in Left ventricular systolic volume with respiration. Inferior vena cava (IVC) diameter, Collapsibility index (CI) in spontaneously breathing patients, and distensibility index (DI) in mechanically ventilated patients of acute pancreatitis can be measured along with the CVP and mean arterial pressure (MAP) to guide fluid therapy. There are few studies on using POCUS-directed fluid resuscitation in patients with acute pancreatitis. Hence this study was carried out exclusively in patients of acute pancreatitis presenting within 72 hours of the onset of pain.

Aims

To determine if CVP correlated with the distensibility index of IVC in mechanically ventilated patients and the collapsibility index in spontaneously breathing patients undergoing POCUS-guided fluid resuscitation.

Methods

A prospective observational study comprising 66 patients with acute pancreatitis was evaluated between January 2016 to April 2018 and POCUS-directed fluid resuscitation was carried out with regular monitoring of IVC parameters, CVP, MAP, and various clinical and biochemical parameters on a 6th hourly basis.

Results

After adequate POCUS-directed fluid resuscitation, there was a significant increase in CVP ($p = 0.0002$) and MAP ($p = 0.0004$) in spontaneously breathing patients and MAP ($p = 0.0001$) and CVP ($p = 0.0118$) in mechanically ventilated patients. There was a negative correlation between CI, MAP, and CVP ($R= -0.7$, $p=0.04$) in spontaneously breathing patients, however, there was no correlation between DI, MAP, and CVP in mechanically ventilated patients ($R= -0.152$, $p=0.06$).

Conclusion

Collapsibility index and IVC diameters are novel noninvasive methods to guide fluid therapy in spontaneously breathing patients of acute pancreatitis, however in mechanically ventilated patients CVP and distensibility indices and IVC diameter showed no correlation, making it unreliable as an accurate marker of intravascular fluid status in mechanically ventilated patients of acute pancreatitis.

Keywords

Inferior vena cava, Central venous pressure, Mean arterial pressure, Ultrasound (POCUS), fluid resuscitation, acute pancreatitis.

INTRODUCTION

In acute pancreatitis, there is extravasation of protein-rich intravascular fluid into the peritoneal cavity and retroperitoneum space causing hemoconcentration and decreased renal perfusion with elevation in Blood Urea Nitrogen (BUN). Subsequently, the decreased perfusion into the pancreas leads to pancreatic necrosis and its various complications. Inadequate fluid resuscitation results in tissue hypoperfusion and worsening end-organ dysfunction. Resuscitation strategies that avoid under-resuscitation have a proven mortality benefit.[1,2] Thus, appropriate fluid administration is a cornerstone in the management of acutely ill patients with acute pancreatitis.[3,4] Measurement of central venous pressure (CVP) by a central-based catheter is used to guide intravascular volume estimation and is the standard of care.

Unfortunately, CVP measurement requires invasive central venous catheters that can be difficult and time-consuming to insert and associated with complications.[1,2]

Echocardiography as a part of POCUS is a rapid non-invasive means of inferring CVP, thus, providing clinicians with an acceptable alternative. Determination of various static and dynamic parameters according to expertise, has changed the practice in intensive care units. It has helped clinicians to differentiate between fluid responders and non -non- responders. POCUS Assessment Includes fluid resuscitation, fluid test, and fluid restriction. POCUS may help to guide adequate fluid resuscitation in patients with acute pancreatitis within the first 72 hours.[5] During the process of resuscitation clinicians usually come up with a situation to differentiate between fluid responders and non-responders. Fluid responsiveness can be assessed based on the resolution of (1) Hypotension (2) Oliguria (3) increased lactate levels. The above-mentioned parameters are not as sensitive as an increase in cardiac output, as sometimes there is a failure in the rise of blood pressure despite all measures due to low systemic vascular resistance, established renal failure, or lactate levels Therefore use of Echocardiography is more preferred method nowadays. However, preference of parameters to be measured by echocardiography again depends on whether the patient is spontaneously breathing or on mechanical ventilation. It also depends on the Echocardiography skills of the intensivist.

POCUS Assessment Includes fluid resuscitation, fluid test, and fluid restriction.

POCUS might help to guide adequate fluid resuscitation in patients with acute pancreatitis within the first 72 hours.[5]

The parameters can then further be divided into Static and Dynamic.

Static parameters

These provide a measurement of single ventricular loading condition.

a. Size of IVC
b. Pulmonary artery occlusion pressure using Doppler indices.
c. Area, volume, and diameter of both the ventricles.

Dynamic parameters

They are more accurate especially in patients on mechanical ventilation as they determine whether the patient is on the ascending limb of the Frank- Sterling curve or the flat portion of the curve.

a. Change in VTI with respiration - a cutoff value of 12 % for maximal velocity and 20 % for respiratory changes are usually considered to differentiate between responders and non-responders. When measured with TEE has high specificity and sensitivity.
b. Change in diameter of IVC and SVC - Both the collapsibility index and Distensibility index can help clinicians differentiate responders from non-responders.
c. Though there are many pitfalls within above mentioned measurements like with respiration there is displacement of the liver and adjacent IVC. In such circumstances, IVC may show a change in size when it shifts out of the ultrasound beam plane but in real there is no change in size. Similarly, during aortic blood flow Doppler sample may move and can give a false indication of respiratory change in aortic blood flow and the size of IVC.
d. Pulmonary artery occlusion pressure using Doppler indices.

e. Area, volume, and diameter of both the ventricles.

A "fluid responder" has been defined as a patient whose cardiac output (CO) increases by 15% in response to a fluid bolus, whereas non-responders either show decreased CO or minimal increase. Pulse pressure variation, stroke volume variation, and systolic pressure variation are established dynamic measures that estimate changes in CO before and after induced fluid shifts into the heart by the cyclic changes caused by respiration. (Caused by mechanical ventilation, passive leg raising, or rapid infusion of small fluid volumes.[6] Although maximal IVC size in healthy patients has a wide range from 9 to 27 mm, there appears to be discriminatory power in identifying small IVC sizes. Conversely, a large absolute IVC diameter, which we have defined as greater than 25 mm, can be consistent with a volume-loaded state unlikely to respond to further fluid resuscitation.[7]

IVC collapsibility index (CI) was calculated as (maximum diameter on inspiration − minimum diameter on expiration)/minimum diameter on expiration and expressed in percentage.CI has a threshold value of 12% and was reported to discriminate with 90% sensitivity and specificity for volume responsiveness.[8] Inferior vena cava distensibility in mechanically ventilated patients. The distensibility index (DI) of the IVC is calculated as the difference between IVC diameter at end inspiration (Dmax) and IVC diameter at end-expiration (Dmin), expressed as a percentage of Dmin, that is, $[(D_{max} - D_{min})/D_{min}] \times 100\%$. A threshold value of 18% for DI was reported to discriminate with 90% sensitivity and specificity for volume responsiveness.[9,10]

An admission hematocrit of more than 44% and failure of hematocrit to decrease in 24 hours have been predictors of necrotizing pancreatitis and elevation of or rising BUN is associated with increasing mortality.[11] Early vigorous IV volume replacement for intravascular resuscitation is of utmost importance

There are not many studies in the literature regarding the correlation between CVP and IVC parameters (collapsibility index in spontaneous breathing, distensibility index in mechanically ventilated, IVC diameter) on the use of POCUS-corrected fluid resuscitation exclusively in patients of acute pancreatitis. Hence this study was planned.

Aims and Objectives

To determine if CVP correlated with the distensibility index of IVC in mechanically ventilated patients and collapsibility index in spontaneously breathing patients of acute pancreatitis who presented within 72 hours of onset of pain and underwent POCUS-guided fluid resuscitation.

Inclusion Criteria

1. Patients of acute pancreatitis mild, moderately severe, and severe based on revised Atlanta criteria 2012 presenting within 72 hours of admission.
2. Patients of acute pancreatitis on spontaneous and CMV (continuous mandatory ventilation) modes of mechanical ventilation were included.

Exclusion Criteria

1. Patients having abdominal compartment syndrome.
2. Patients on mode of ventilation other than mentioned in the inclusion criteria.
3. Pregnancy.
4. Other causes of raised intra-abdominal pressure,

5. Patients in whom USG could not be done because of poor echo window or dressings,
6. Acute coronary syndrome, cardiac dysrhythmias (as a primary diagnosis), congestive heart failure, pulmonary embolism, status asthmaticus.

METHODS

A prospective, observational study was carried out at SMS Medical College and Hospital, Jaipur. 66 patients with acute pancreatitis on spontaneous ventilation and who needed ventilatory support (invasive or noninvasive) and fulfilled inclusion and exclusion criteria from January 2016 to April 2018 were enrolled in the study.

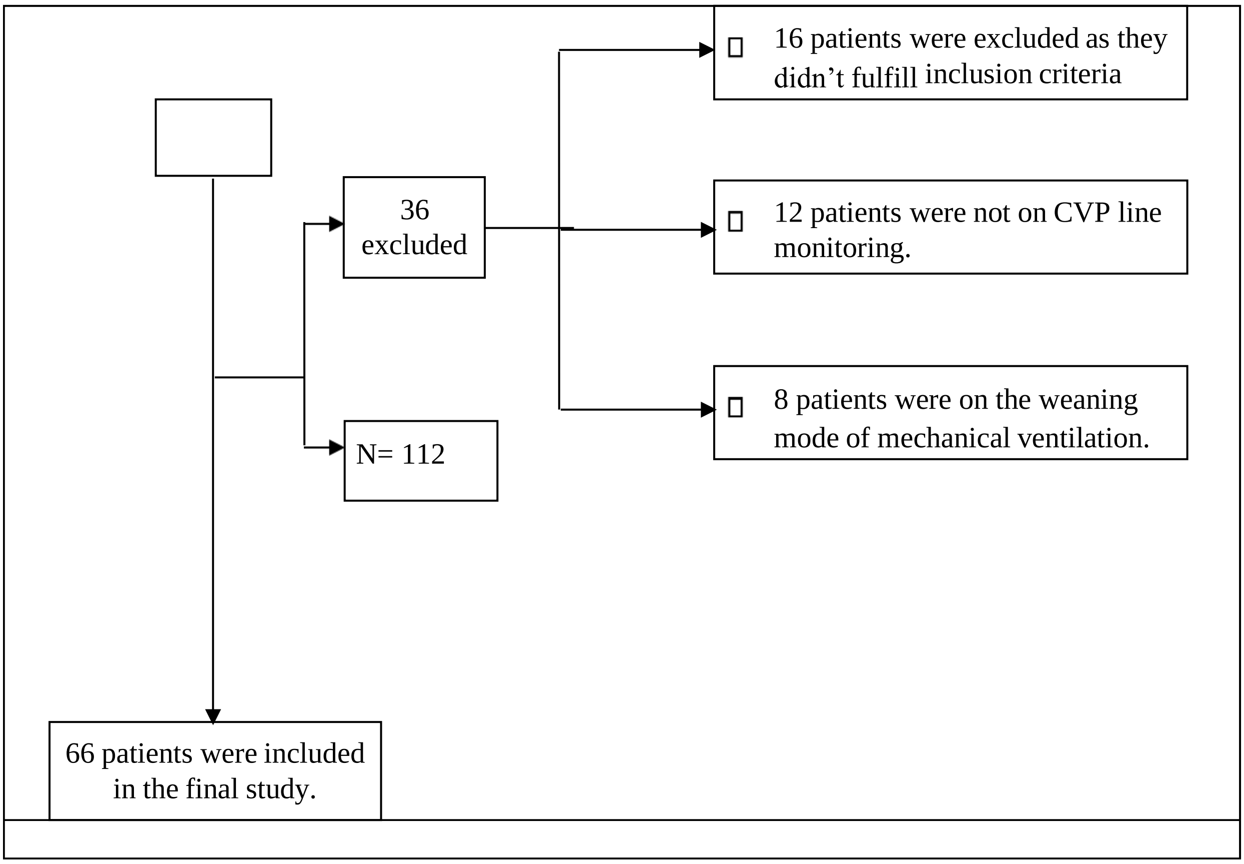
A target resuscitation strategy with aggressive hydration with 250-500ml/hour of isotonic crystalloid solution preferably Ringers lactate was undertaken unless cardiovascular, renal, or other related comorbid factors existed. Measurement of hematocrit, Blood Urea Nitrogen (BUN), Inferior vena cava (IVC) diameter, Collapsibility index (CI) in spontaneous breathing, and Distensibility index (DI) in mechanically ventilated patients, and central venous pressure (CVP) were noted on every 6 hours as a guide to monitor response to therapy. Once adequate IVC diameter was obtained by definition 25mm or C.I <12% / D.I <18% respectively. Patients were then fluid resuscitated with a target of hourly urine output of 0.5ml/Kg/hour or a target of maintaining IVC diameter and Collapsibility index <12% / DI <18%, by 6th hourly measurements spontaneously and mechanically respectively. A lack of improvement in CI/DI index, IVC diameter, hematocrit, and Blood urea nitrogen (BUN) during serial measurement was treated with volume challenge with increasing fluid rate of 1.5 ml/kg/hour till targets were achieved. Vasopressors were started in situations of non- achievement of desired mean arterial pressure (MAP >=65mmHg) despite reaching endpoint CVP or IVC CI/DI target parameters.

Following admission to the ICU, those patients requiring mechanical ventilation were put on ventilatory support, and central venous catheterization was done. Ventilatory mode and positive end-expiratory pressure (PEEP) applied were recorded for each patient. Patients on mechanical ventilation in CMV mode having tidal volume 8ml/kg, PEEP equal to 4, and rate 14 breaths/min were included in the study.[11,12] Echocardiography was carried out, to assess cardiac contractility and to rule out congestive heart failure. CVP was measured by central venous catheters inserted in the internal jugular vein with its tip positioned in the superior vena cava just proximal to the right atrium. It was measured at zero point which corresponds with the phlebostatic axis. The CVP was measured in the end-expiratory phase of respiration using a column of saline which was later converted into mmHg by dividing it by 1.3.

The IVC assessment was made using a Philips EPIQ7 ultrasound machine with the patient in the supine position using an acoustic window inferior to the xiphoid, angling to the right. The cross-sectional image of the IVC was visualized at the right atrial/hepatic vein/IVC junction and then rotated so that a long-axis view of the IVC was obtained.

M-mode was applied at approximately 1 cm distal to the IVC-hepatic vein junction where the anterior and posterior walls were visualized. Maximum and minimum diameters of IVC were measured in each respiratory cycle. The recordings were taken by an intensivist and later cross-checked by a cardiology resident, who was blind to the study.

Following bladder drainage by a Foley urinary catheter while the patients were in the supine position, 50-100 ml of isotonic fluid was injected into the bladder under sterile conditions and the distal portion was clamped. Subsequently, an 18-gauge needle was entered



into the output of the urinary catheter and was connected to a 3-way system and a water manometer. After, being filled with sterile fluid, the patient side of the manometer was opened. The "0" point of the manometer was aligned with the patient's pubic symphysis point and the point where the liquid column was read in cm. Thus, the urinary bladder pressure (UBP), which indirectly reflected the intra-abdominal pressure was determined in cm of water. Patients with an intra-abdominal pressure over 12 cm of water were excluded from the study.

Statistical Analysis

The statistical analysis was performed using a statistical package for social sciences (SPSS) version 23.0 for Windows (SPSS, Chicago IL, USA). Data were expressed as absolute numbers, percentages for categorical variables, and mean± standard deviation. Ranges were calculated for continuous variables as appropriate. Student t-test, Pearson coefficient of correlation was used to assess if CVP correlated with collapsibility index in spontaneously breathing patients and distensibility index of IVC in mechanically ventilated patients respectively in POCUS-guided fluid therapy in patients of acute pancreatitis who presented within 72 hours of onset of pain.

OBSERVATIONS

The trend in urine output (UO), Mean arterial pressure (MAP), and Central venous pressure (CVP) Collapsibility Index (CI) were plotted. Table no. 1 shows the baseline characteristics of the patients and Table no. 2 shows the mean collapsibility index at 0 and 48 hours in spontaneously breathing patients, their respective mean CVP and MAP at 0 and 48 hours post fluid resuscitation. Figure 1A illustrates the correlation between CVP and CI in spontaneously breathing patients and Figure 1B illustrates the correlation between CVP and DI in mechanically ventilated patients. Figures 2, 3, 4, and 5 represent the trends of MAP, CVP, UO CI, and DI in spontaneously breathing and mechanically ventilated patients respectively through the 48 hours. After adequate POCUS-directed fluid resuscitation, there was a significant increase in CVP (p = 0.0002) and MAP (p = 0.0004) in spontaneously breathing patients and MAP (p = 0.0001) and CVP (p = 0.0118) in mechanically ventilated patients. Figure 1A demonstrates there was a negative correlation between CI, MAP, and CVP (R= -0.7, p=0.04) in spontaneously breathing patients, However, Figure 1B showed no correlation between DI, MAP, and CVP in mechanically ventilated patients (R= - 0.152, p=0.06).

Total number of patients – 66 Mean age 42.5+-15.1 years			
Severity of Pancreatitis number of patients	Mild	moderate	severe
	4	42	20
Etiology of Pancreatitis number of patients	ethanol	gallstone	others
	50	10	6
Sex number of patients	Male	female	
	60	6	
Ventilation mode number of patients	spontaneous		mechanical
	42		24

Table 1 - Baseline characteristics of the patients

Spontaneous ventilation				Mechanical ventilation			
	0 hrs	48 hrs	P value		0 hrs	48 hrs	P value
CI	11.9 +- 6.6	10.3 +- 5.1	0.0006 (P<0.05)	DI	20.74 +- 1.8	17.2+- 2.3	0.01(P<0.05)
Mean CVP(cm)	8.3 +- 5.2	13.9+- 3.7	0.0002 (P<0.05)	Mean CVP(cm)	9.1+- 1.2	11.5+- 2.3	0.01(P<0.05)
MAP	87.9 +- 9.5	98.8+- 6.7	0.0004 (P<0.05)	MAP	70.5+- 6.0	90.4+- 9.8	0.0001(P<0.05)

Table 2 – Correlation of POCUS parameters CI in spontaneously breathing and DI in Mechanical ventilation with Mean CVP and MAP

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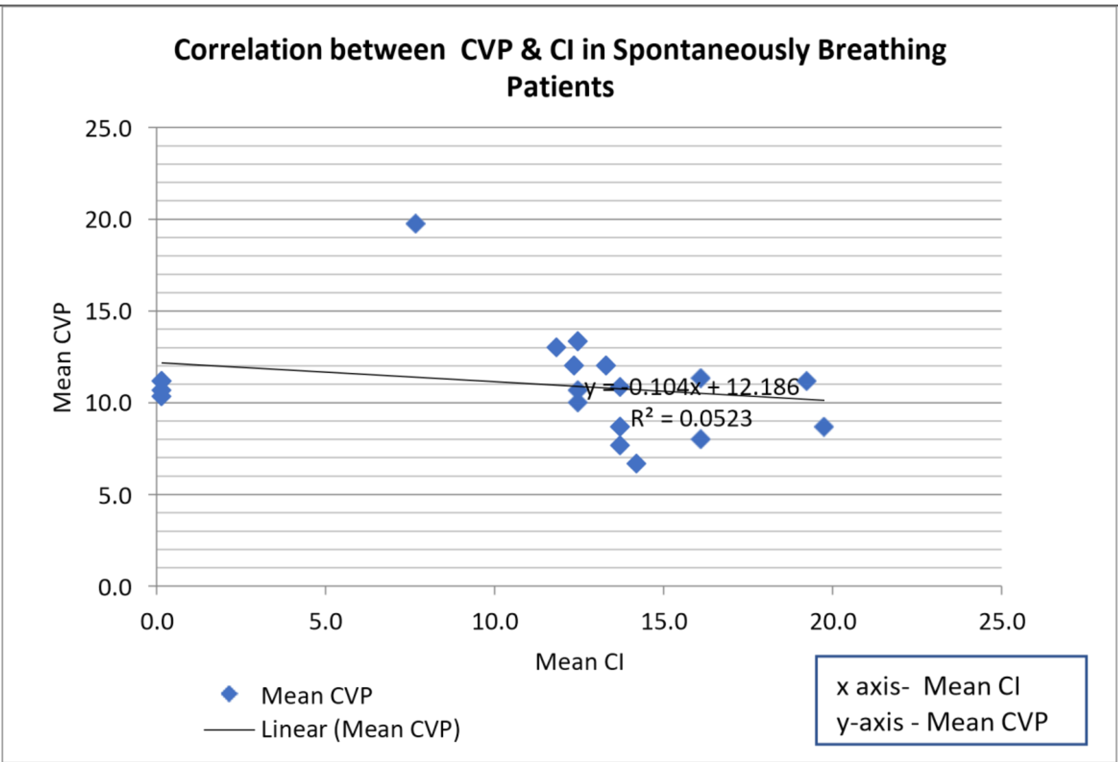
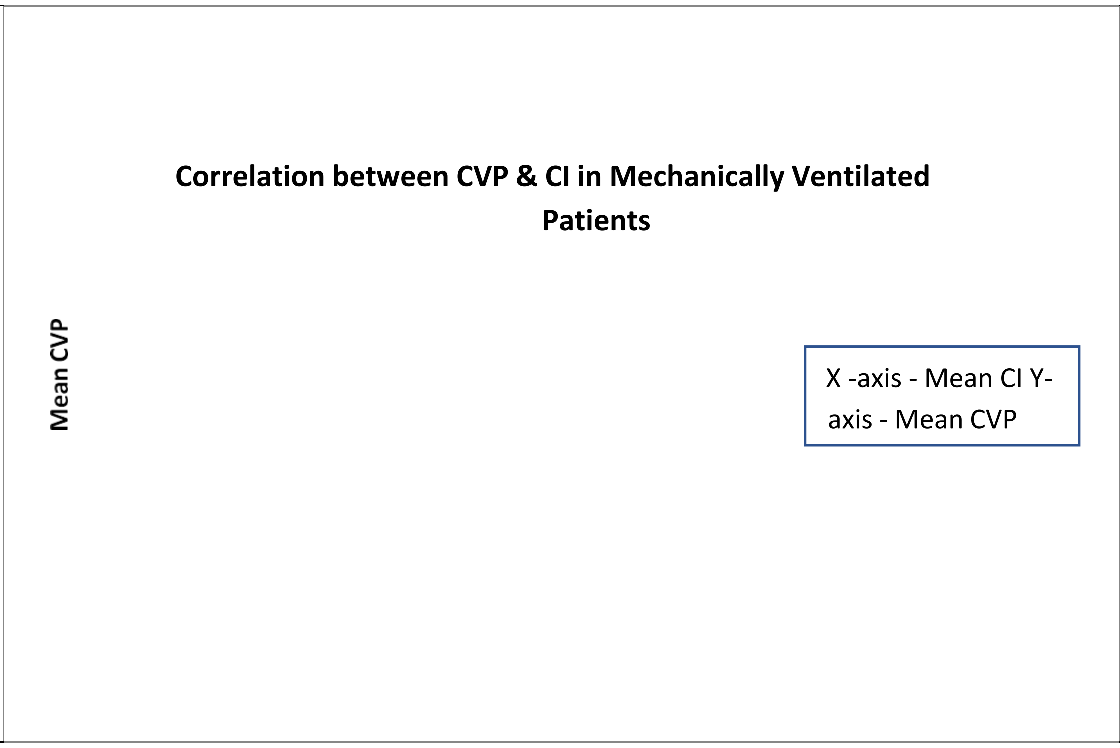


Figure 1A – Correlation between CVP and CI in Spontaneously Breathing Patients

CVP – central venous pressure, CI – collapsibility index

The correlation between CVP and CI in spontaneously breathing patients is significant (the slope of the graph is R=0.052, P<0.05)



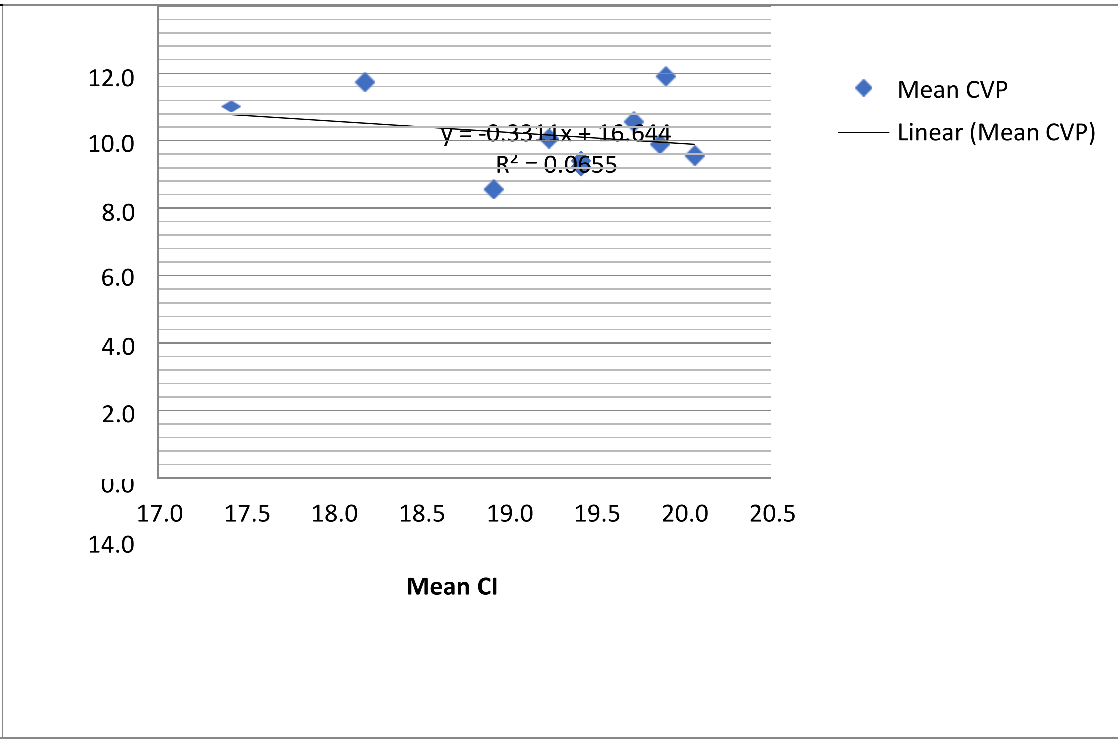


Figure 1B – Correlation between central venous pressure (CVP) and collapsibility index (CI) in Mechanically Ventilated Patients

CVP – central venous pressure, CI – collapsibility index

The correlation between CVP and CI in mechanically ventilated patients is significant (the slope of the graph is R=0.065, P<0.05)

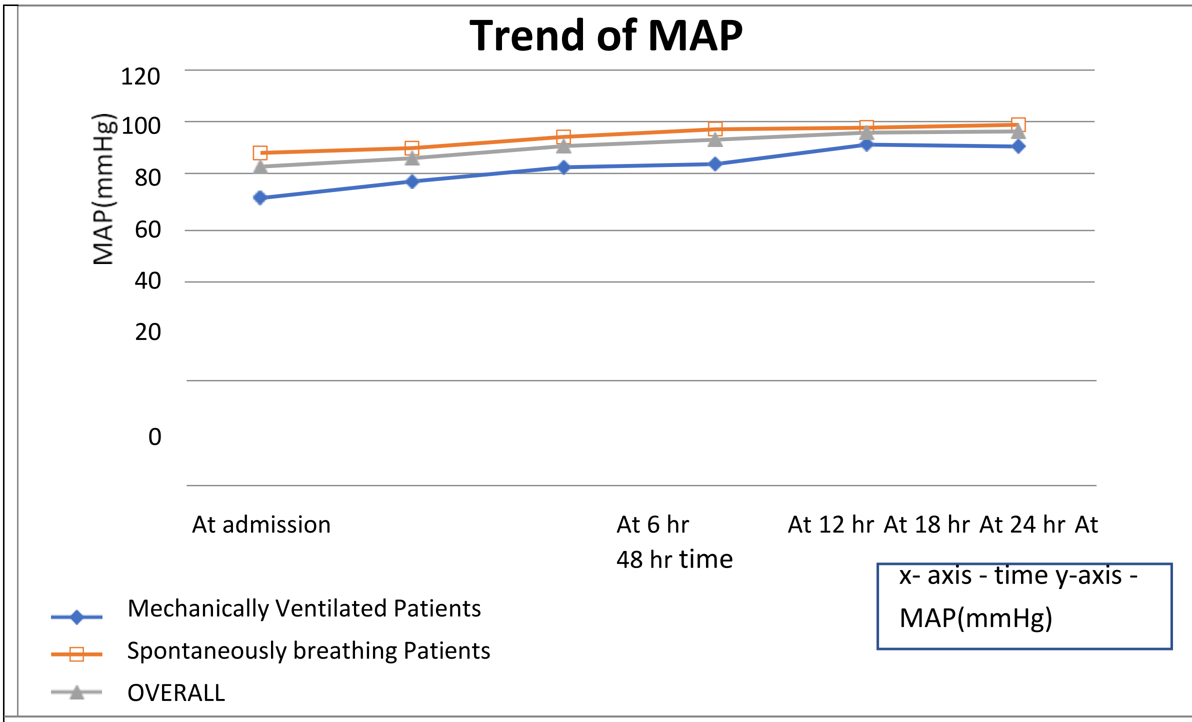


Figure 2 – Trend of Mean arterial pressure (MAP) in acute pancreatitis patients on spontaneously breathing and mechanical ventilation

MAP – mean arterial pressure

Shows as the patients are volume resuscitated the Mean arterial pressure tend to rise and achieves the plateau around 48 hours.

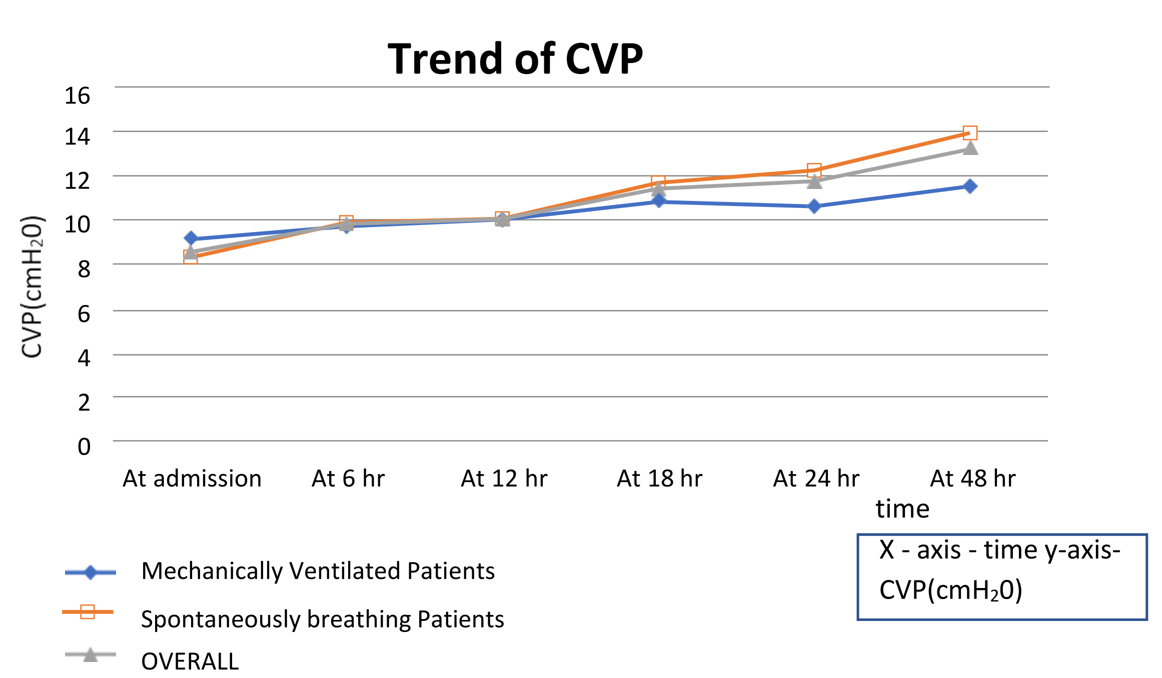


Figure 3 - Trend of Central venous pressure (CVP) in acute pancreatitis patients on spontaneously breathing and mechanical ventilation

CVP- central venous pressure

As seen in the graph the CVP tends to rise and plateau off within 48 hours.

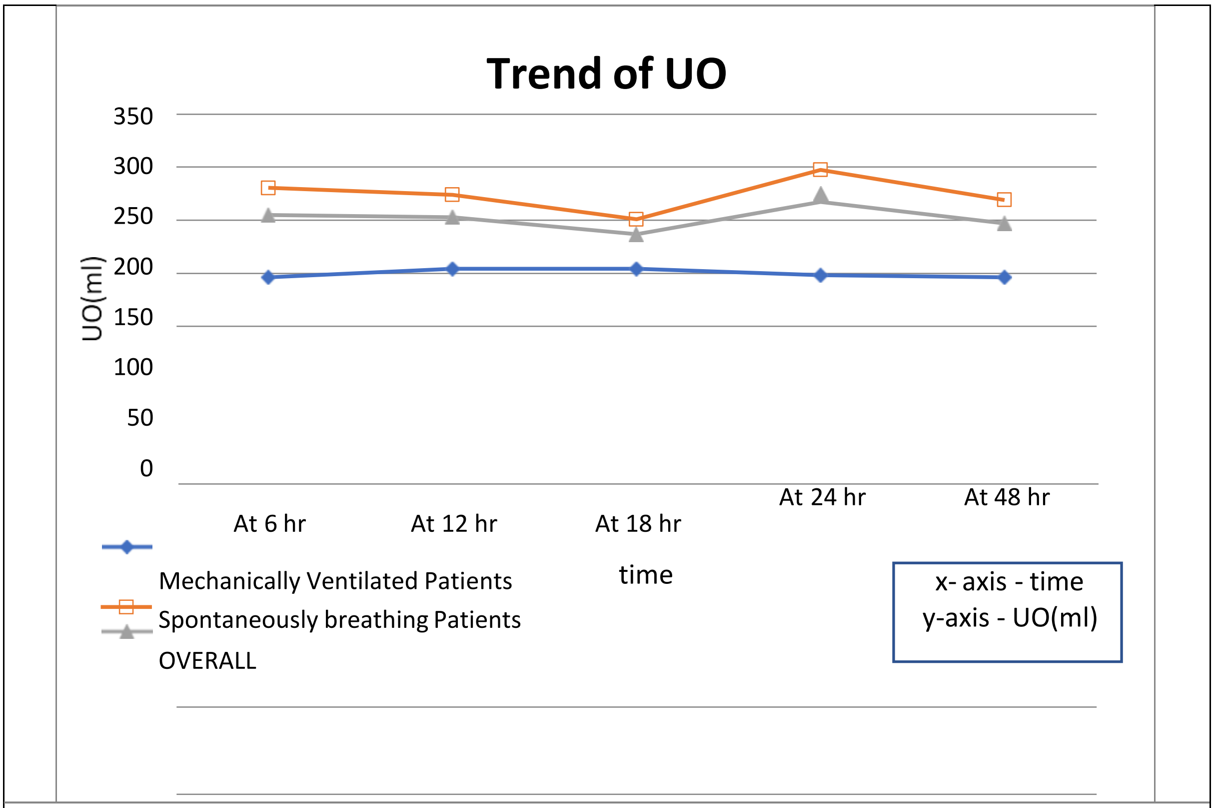
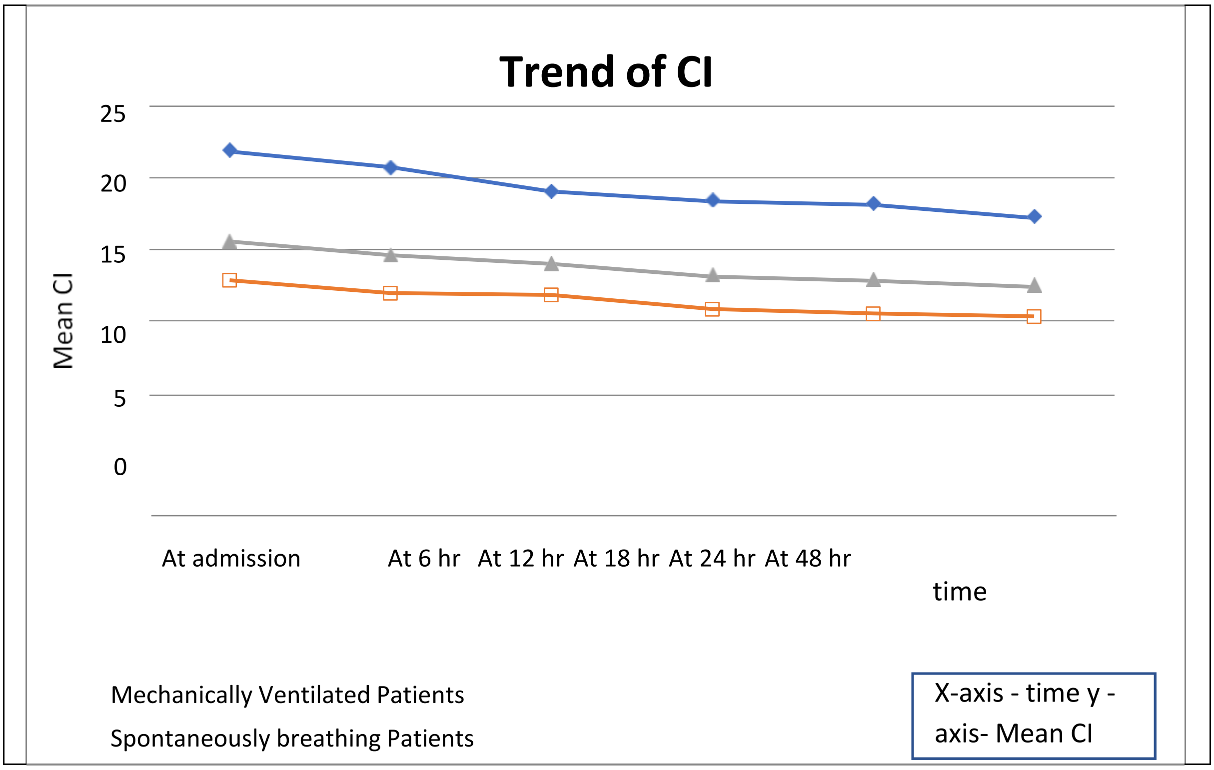


Figure 4 - Trend of Urinary output (UO) in acute pancreatitis patients on spontaneously breathing and mechanical ventilation

UO- urine output



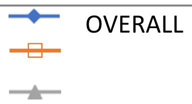


Figure 5 – Trend Of Collapsibility index (CI) and Distensibility index (DI) Verses Time in patients on Spontaneous Breathing And Mechanically Ventilated Patients Respective

CI – collapsiblity index

As the fluid resuscitation continues the CI and DI falls over time.

DISCUSSION

Our study group included patients having exclusively acute pancreatitis and this study evaluated the POCUS-directed fluid therapy's effects on the CVP and IVC indices and their correlation in spontaneously breathing and mechanically ventilated patients respectively, whereas other studies in critical care settings included different and diverse study groups which were heterogenous such as hemodialysis patients, patients with hemorrhagic shock due to trauma, patients during cardiac surgery with ongoing conditions.

In our study there was a negative correlation between the CVP and CI in spontaneously breathing acute pancreatitis patients, demonstrating the fact that as fluid response improves Collapsibility index decreases and Mean arterial pressure and Central venous pressure rise. These observations were similar to other studies which showed CI > 50% had a strong association with a lower CVP < 8 mmHg,[2] whereas CI < 50% indicated raised RA pressures of more than 10 mmHg,[13] thus documenting that the combination of both collapsibility indices (CI) and IVC diameter measurements may assist in improved ultrasonographic evaluations of the IVC with clinically important categories of right atrial pressure (e.g. 0–10 mmHg).[14] Collapsibility Index (CI) strongly correlates with low (< 20%) and high (> 60%) CVP values and suggests that the closer the CI is to 0% or 100%, the more the probability that the patient is either volume-overloaded or volume-depleted, respectively. No such evidence supports a linear relationship between CI and CVP; however, there is an inverse relationship between CVP with CI when CI values are either very high or low. The ability to predict CVP values precisely is of untested clinical gain, keeping in view the poor performance of CVP as a marker of intravascular volume and fluid responsiveness. A very high CI (often associated with a very low CVP) may serve as a rational sign that it is harmless to give more fluid without volume overload.[15]

In our study, in 24 mechanically ventilated patients, however, there was no statistically significant relationship between IVC diameters measured by ultrasonography at the end of expiratory and inspiratory phases and measured CVP values at the same phases.

In our study the PEEP was maintained in the majority of patients within the range of 0-5 mmHg however few patients have required higher PEEP during their therapy thus accounting for the lack of correlation between CVP and distensibility index in mechanically ventilated patients, these observations are similar to meta-analysis done by other *authors*, who observed that the correlations between IVC dimension and CVP in mechanically ventilated patients were generally weak and inconsistently observed. Furthermore, the use and magnitude of PEEP varied greatly across studies on IVC diameters and DI in mechanically ventilated patients. Positive pressure ventilation leads to increased intrathoracic pressure, decreased systemic venous return, and increased volume of venous blood in the IVC. The dimension and distensibility of the IVC are consequently affected. Therefore, the use of IVC measurements to estimate right atrial pressure (RAP) in mechanically ventilated patients is usually unreliable. pressure less than 10mmHg. Therefore, a small IVC in the setting of mechanical ventilation may still point toward the absence of elevated RAP. In addition, the correlation of IVC, DI, and RAP may still be valid in the absence of PEEP. The above discussion can explain the lack of significant correlation between DI, MAP with CVP in mechanically ventilated patients.

Thus, measuring the IVC diameter using POCUS is a novel method to guide fluid resuscitation protocols in acute pancreatitis in spontaneously breathing patients, however, IVC diameter measurement becomes inconsistent in mechanically ventilated patients with higher PEEP. Thus, measurement of collapsibility index in spontaneously breathing patients in guiding fluid therapy correlated inversely with CVP and MAP thus demonstrating its utility however the lack of correlation between DI, CVP, and MAP in mechanically ventilated patients makes DI an unreliable marker of intra-intravascular fluid status in mechanically ventilated patients of acute pancreatitis. VTI measured in this group of patients might be more accurate.

Limitations

The main limitation of our study is related to its observational nature small sample size and the exclusion criteria narrowing the patient group. Lung POCUS and VTI measurements are sophisticated measurements requiring higher training, hence were excluded; as the IVC diameters can be measured with ease by beginners and emergency doctors alike.

CONCLUSION

POCUS-directed fluid resuscitation is a novel non-invasive way to guide fluid therapy in acute pancreatitis. Collapsiblity index and IVC diameters are novel noninvasive methods to guide fluid therapy in spontaneously breathing patients of acute pancreatitis, however in mechanically ventilated patients CVP and distensiblity indices and IVC diameter showed weak correlation, thus making it unreliable as an accurate marker of intravascular fluid status in mechanically ventilated patients of acute pancreatitis.

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