Original Article

Impact of Integrated Cardiopulmonary Ultrasound on Clinical Outcome of Shocked Patients in Intensive Care Unit

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ABSTRACT

Background: With the decreasing utilization of invasive hemodynamic monitoring, bedside-focused ultrasound had emerged as a valuable adjunct in the assessment and treatment of patients experiencing shock.

Purpose: The aim of the current study is to assess the heart and lung conditions in shocked patients using focused cardio-pulmonary ultrasound for treatment guidance and their implication on the patient's outcome.

Methods: This randomized prospective case control study was conducted on 108 shocked cases. The primary outcome included mortality rate, 72 hours after the initial fluid resuscitation. Secondary outcomes included duration of intensive care unit (ICU) stay, duration of mechanical ventilation, frequency of acute kidney injury and correlation between ultrasound variables with mortality rate.

Results: This study revealed that 72-hour mortality rate in group (A) was 46.3%, compared with 25.9% in group B (*P*= 0.027). A strong positive correlation was reported among 72-hour mortality and IVC diameter, LUSS, EPSS, APACHE II score and serum lactate. PaO_2/FiO_2 was negatively related with mortality. Group A revealed a significantly more extended duration of ICU stay compared with group B (7.89 vs 5.83 days, *P*<0.001) respectively. The mean duration of mechanical ventilation in group (B) was 68.31 hours and 81.82 hours in group (A) (*P*= 0.035).

Conclusions: This study revealed a significant decline in 72-hour mortality rate in ultrasound treated patients' group, in comparison with the standard treated patients' group. Integrated cardiopulmonary ultrasound resulted in shorter ICU stay and mechanical ventilation.

Key Words: Cardiopulmonary ultrasound, Correlation, Mortality, Shock.

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INTRODUCTION

Shock is a prevalent medical condition that impacts approximately one-third of critically ill patients in ICU. It diminishes the delivery of oxygen and nutrients to the substantial organs and is strongly correlated with an elevated risk of death[1]. Evaluation of hemodynamic status and management strategies for acute circulatory shock continue to be complex challenges in the fields of emergency medicine and critical care. With the decreasing utilization of invasive hemodynamic monitoring, bedside-focused US has emerged as a valuable adjunct in the assessment and treatment of patients experiencing shock[2].

Integrating bedside ultrasonography in patients with undifferentiated shock enables fast assessment of reversible reasons for shock and enhances precise diagnosis in undifferentiated hypotension[3]. The critical care ultrasound (CCUS) is commonly recommended as the primary method for evaluating hemodynamics and properly quantifying pathophysiological changes associated with shock, which might be utilized to guide shock therapy. Current protocols lack specificity by not including specific variables like Ejection Fraction (EF), Mitral Annular Plane Excursion (MAPSE), Tricuspid Annular Plane Excursion (TAPSE), Inferior Vena Cava (IVC), End Point Septal Separation (EPSS), and Lung Ultrasound Score System (LUSS) as indicators[1].

CCUS examination conducted by qualified physicians offers vital insights to help caregivers comprehend the detailed features of hemodynamics and lung pathology upon admission to ICU. Key factors acquired using CCUS can help predict patients' prognosis and should be given

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greater consideration in clinical decision-making. Lung ultrasonography is commonly employed for identifying various pulmonary conditions such as pneumonia, connective tissue disorders, and interstitial lung illnesses. In ICU, close monitoring of lung pathologic alterations is prioritized to inform treatment decisions for patients. Lung injuries from inflammation, trauma, or water accumulation always result in infiltration, leading to the loss of lung air. Various ultrasonography indicators are produced during examination in each section of the lung, based on the extent of aeration loss and water accumulation. LUSS is a semiquantitative score that evaluates lung aeration loss due to various lung pathologic alterations as pneumonia, atelectasis, pleural effusion, and lung edema. It is calculated by summing the values of each test zone[4]. The aim of current research is the assessment of the heart and lung conditions in shocked patients using focused cardio-pulmonary ultrasound for treatment guidance and their implication on the patient's outcome.

PATIENT AND METHODS

This randomized prospective case control study was conducted on 108 shocked cases in ICU, Al-Azhar university hospitals, from March 2022 till September 2023.

Primary and secondary outcome:

Primary outcome included mortality rate, 72 hours after the initial fluid resuscitation. Secondary outcomes included duration of ICU stay, duration of mechanical ventilation, frequency of acute kidney injury and correlation between ultrasound variables with mortality rate.

Eligibility Criteria:

All patients of both sex with age >18 years old admitted to ICU suffering from shock (within 6 hours) were involved in the research. The shock inclusion criteria are one of the following: state of hypotension represented by systolic BP <90mmHg or MAP <60mmHg), and positive with any of the following conditions: Lactate concentration is greater than 2mmol/L; capillary refill time exceeds 4.5 seconds; urine production per hour is less than 0.5ml/kg. Clammy skin, chilly limbs, and unconsciousness may need the use of intravenous vasopressors.

Cases were excluded if they fulfilled any of the following criteria: Patients with a history of trauma, suspected or diagnosed elevated intra-abdominal or intrathoracic pressures due to various medical conditions, and those with specific cardiac or neurological issues, as well as individuals who declined to take part in the research.

Randomization:

Shocked cases were classified randomly into 2 equal groups, utilizing computer-generated random table.

Group A: Control group (*n*= 54) Patients underwent standard treatment methods i.e., without any use of point of care cardio-pulmonary US scans for guidance of the management.

Group B: Study group (*n*= 54) Patients underwent cardio-pulmonary ultrasound guided management.

Procedure:

Every case in both groups received an immediate treatment, including oxygen therapy, vascular access, and fluid resuscitation. The intervention group utilized clinical signs and doppler ultrasonography to guide fluid and vasoactive management steps, while the control group relied solely on clinical indicators. The patient had an initial clinical assessment and received rapid resuscitative treatments such as establishing an intravenous line and providing fluids, following established medical guidelines. The admission diagnosis was established using standard methods, such as medical history, ECG, and a range of laboratory investigations involving ABG, CBC, blood chemistry (involving liver and renal function tests, serum electrolytes like Na^+, K^+, Cl^-, Ca^{++}, coagulation profile, blood sugar), and necessary radiological examinations. Equipment for bedside sonographic evaluation was promptly provided without any disruption to patients' initial treatment. Standard ventilatory settings were implemented as needed.

Cardiopulmonary Ultrasound (CPUS):

Individuals were scheduled to have echocardiogram (Echo) and lung ultrasonography (LUS) examinations within 6 hours of admission. An eight-zone lung ultrasound assessment approach was used to assess lung pathophysiological changes in shock patients, according to international evidence-based guidelines for point-of-care lung ultrasound. The anterior lateral zones, defined by the anterior axillary lines, were separated into upper and lower parts on both sides of the lungs. The LUS test was essential for identifying lung sliding, lung point, A lines, B lines, consolidation/atelectasis, and pleural effusion (Figure 1). The LUS patterns at every exam location were evaluated based on specific criteria. The scoring system is: 0 points for lung sliding with A lines or less than two isolated B lines, a single point for numerous well-defined B lines (B1 lines), 2 points for several coalescent B lines (B2 lines), and 3 points for lung consolidation. The most prominent ultrasound patterns were recorded in each area, resulting in a cumulative score of 24[1].

Measuring Tricuspid Annular Plane Systolic Excursion (TAPSE):

All patients were placed in the left lateral decubitus posture to get a clean apical 4-chamber picture of the heart. A sampling spike in M-mode was placed at the right lateral border of the heart close to the tricuspid valve annulus, generating real-time B and M-mode tracings at the same time. The TAPSE value was determined by measuring the vertical distance among the peak and trough during one cardiac cycle to evaluate the shortening from apex to base

(Figure 2). Patients were classified into three groups based on TAPSE values: below 16 mm, between 16mm and 20mm, and beyond 20mm[5].

Measuring Mitral Annular Plane Systolic Excursion (MAPSE):

The posture is the same measuring TAPSE. The technique differs in tracing a continuous line of systolic movement from the lateral annulus of the mitral valve to the apex of the left ventricle., normal range of 12 – 16mm (Figure 3). Patients with MAPSE of less than 10 mm was considered abnormal[6].

Measuring E-Point Septal Separation (EPSS):

In order to conduct M-mode measurements of the EPSS, the researchers acquired an independent parasternal long-axis view (Figure 4). The shortest distance (in millimeters) between the apex of the anterior mitral valve leaflet and the interventricular septum was utilized to determine dimensions during early diastole, normal value of EPSS is less 7mm. while values between 7 – 12mm correlate with moderate reduced left ventricular function. Values more than 12mm correlate with severely impaired left ventricular function[7].

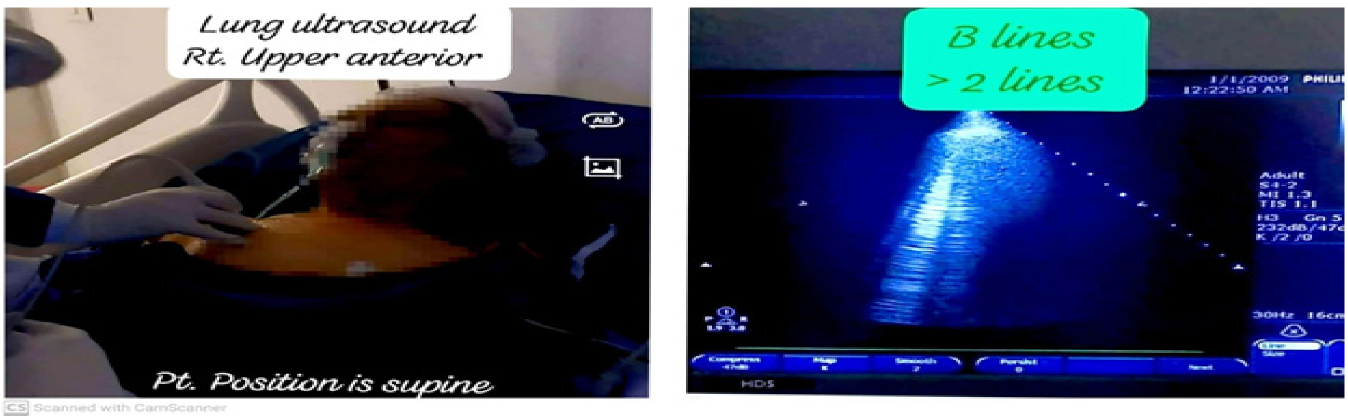

Fig. 1: Lung ultrasound and B line identification.

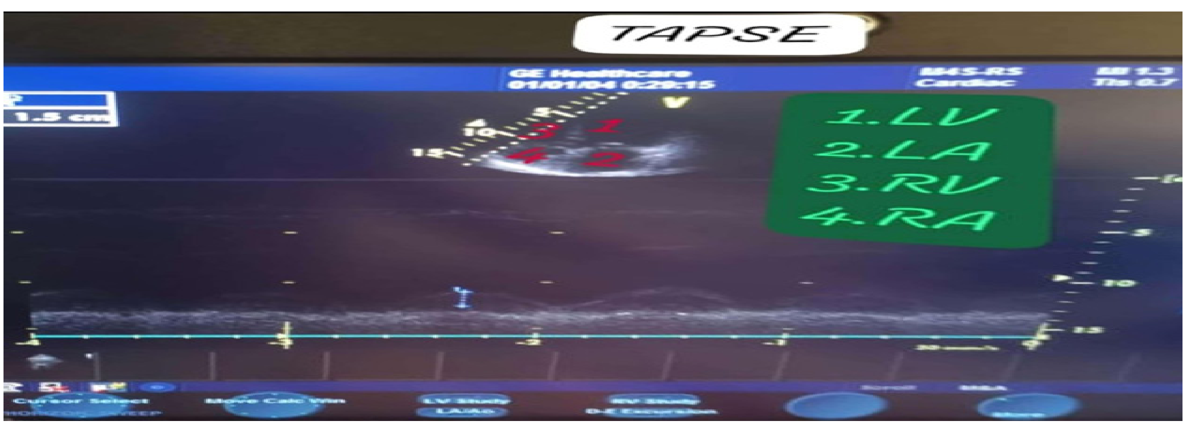

Fig. 2: Measurement of TAPSE (blue line).

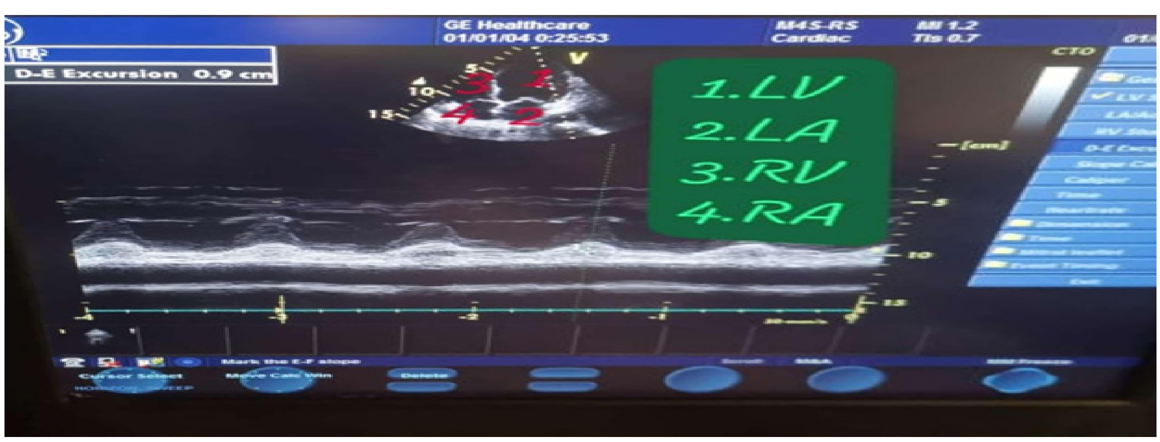

Fig. 3: Measurement of MAPSE.

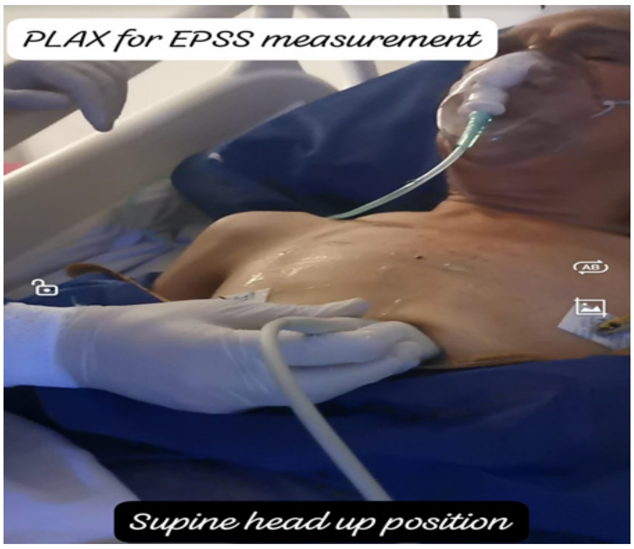

Fig. 4: Parasternal long axis Echo measurement of EPSS.

Measuring IVC:

Volume responsiveness was determined by utilizing the diameter and distensibility index of the inferior vena cava (dIVC). IVC-DI was evaluated using an ultrasound curvilinear low-frequency (2-5 Hz) probe. The IVC-DI was determined utilizing the formula: IVC-DI= [(maximum diameter during inspiration–minimum diameter during expiration) / minimum diameter during expiration]. Subcostal four-chamber and IVC long-axis view: The diameter of the IVC was measured two cm from the junction with the right atrium at the conclusion of expiration. If IVC diameter is less than 1cm, or if the IVC diameter is between 1-2cm and the ditensibility index (dIVC) is greater than 18%, it suggests hypovolemia. When the diameter of IVC is greater than 2cm, or dIVC is less than 18% with an IVC diameter of 1-2cm, it suggests hypervolemia[1].

Statistical Aanalysis:

The sample size was measured utilizing Epi-info TM version 7.2.4.0 (2020). Considering 95% confidence level, 90% power, and according to the data retrieved from Li *et al.,* (2021), the minimum sample size required was 98 patients. An increase of 10% (approximately 10 patients) for dropout, the study investigated 54 patients in each group to test the hypothesis. Percent of exposure was 40% in control, 80% in case, and odds ratio was[4].

The recorded outcomes were analyzed utilizing SPSS version 23.0, a statistical software designed for social sciences by SPSS Inc. in Chicago, Illinois, USA. The quantitative data with normal distribution was revealed as Mean±SD. Variables that deviated from a normal distribution were identified using the median and inter-quartile range (IQR). Furthermore, qualitative features are expressed quantitatively by numerical values and percentages. The Independent-samples *t*-test is used to analyze the means of two parametric variables, whereas the Mann Whitney *U* test is appropriate for comparing non-parametric variables. The Chi- square test was employed to contrast groups with categorical data. The correlation involving cardiopulmonary ultrasound variables and mortality rate was assessed using Pearson correlation test. The Kaplan-Meier technique was employed to illustrate the hazard of patient mortality from the initiation of the trial till the day of death. A 95% confidence interval was established with a corresponding margin of error of 5%. *P*-value <0.05 deemed significant.

RESULTS

Protocol registration in ClinicalTrial.gov is complete, with ID; NCT06295445. This study prospectively enrolled 108 shocked patients. Figure (5) depicted the CONSORT schematic diagram, illustrating progression of the study approach. There was no significant disparity in age, sex, and chronic health issues between study groups, as indicated in Table (1).

This study revealed that the 72-hour mortality rate in group (A) was 46.3%, contrasted with 25.9% in group B (*P*= 0.027) (Table 2). Figure (6) illustrated the Kaplan Meier estimate of 72 hours of mortality among the 2 groups.

Table 1: Comparison between the two groups regarding patients' characteristics:

Parameter	Group (A) (*n*= 54)	Group (B) (*n*= 54)	*P* Value
Age (yrs.)	56.72±11.153	55.57±13.552	0.632#
Sex (Male/Female)	30/24 (55.6/44.4%)	32/22 (59.3/40.7%)	0.846^
Medical Disease:			
• Diabetes Mellitus.	12(22.2%)	10(18.6%)	
• Hypertension.	20(37)	18(33.4%)	
• Chronic Pulmonary Disease.	2(3.8%)	8(14.8%)	>0.05
• Coronary Artery Disease.	2(3.8%)	10(18.6%)	
• Renal Disease.	16(29.6%)	6(11.2%)	
• None.	2(3.7)	2(3.7)	

Data are represented as Mean±SD or number and percentage as appropriate; #: Student *t* test; ^: Chi-square test.

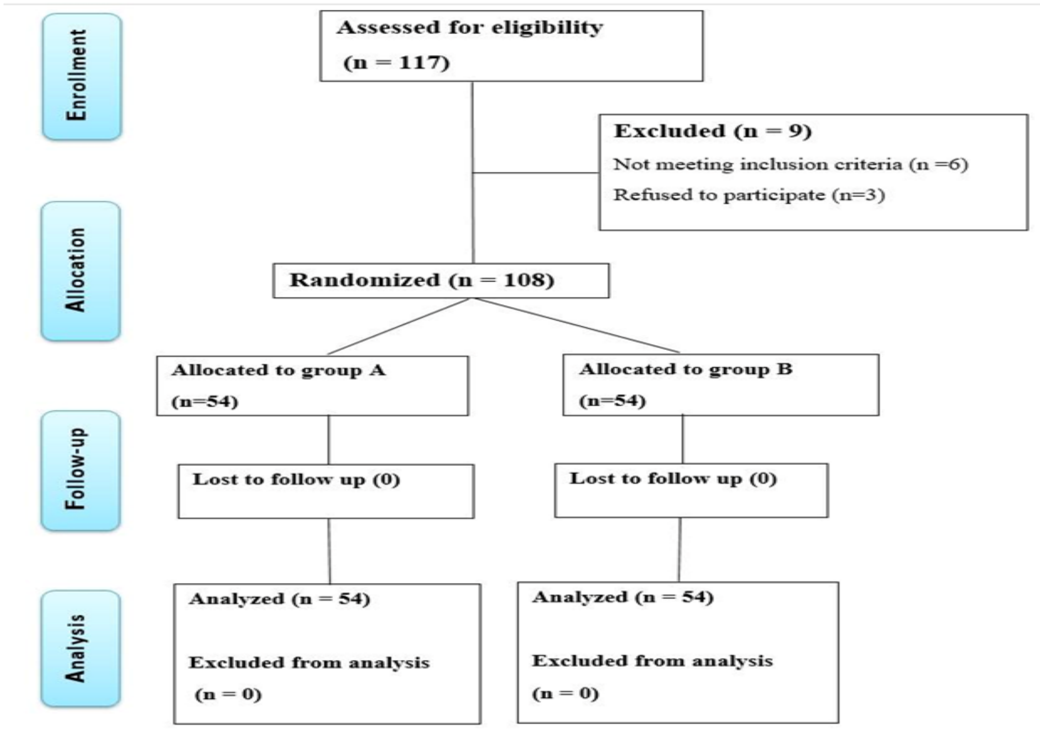

Fig. 5: CONSORT flow diagram of the study process.

Table 2: 72-hour mortality rate comparison between two groups:

72 hours Mortality rate	Group (A) (*n*= 54)		Group (B) (*n*= 54)		X^2	*P* Value
	No.	%	No.	%		
Survival	29	53.7	40	74.1	4.856	0.027*
Died	25	46.3	14	25.9		

*: Statistically significant at P<0.05, X^2: Chi-square test.

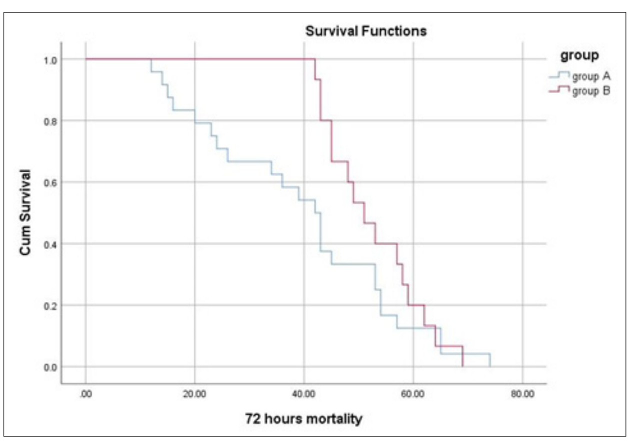

Fig. 6: Kaplan Meier estimate of 72 hours of mortality among the two groups.

In addition, this study showed a strong positive correlation (r) among 72-hour mortality and IVC diameter, LUSS, EPSS, Acute Physiology And Chronic Health Evaluation (APACHE II) score and serum lactate. PaO_2/FiO_2 was negatively related with mortality (r= 0.155, P= 0.04) (Table 3).

Table 3: Correlation between ultrasonic variables, PaO_2/FiO_2, lactate to 72-hour mortality:

Parameter	72-hours Mortality	
	Pearson Correlation	*P* value
Sex	0.011	0.888
Age	0.117	0.123
TAPSE	0.103	0.175
MAPSE	0.071	0.351
Diameter of IVC	0.18	0.001*
LUSS	0.16	0.001*
EPSS	0.24	0.001*
APACHE II	0.28	0.001*
Heart rate	0.098	0.194
MAP	0.105	0.164
Lactate	0.14	0.015
PaO_2/FiO_2	0.155	0.041

*: Statistically significant at P<0.05; TAPSE: Tricuspid annular plane systolic excursion; MAPSE: Mitral annular plane systolic excursion; IVC: Inferior vena cava; LUSS: Lung Ultrasound Severity Score; EPSS: E-Point Septal Separation; MAP: Mean arterial pressure.

Moreover, acute kidney injury was more prevalent in group A, contrasted with group B (27.7 vs 18.5 %, P= 0.15) (Table 4). Group A revealed a significantly more extended duration of ICU stay contrasted with group B (7.89 vs 5.83 days, P<0.001) respectively. Similarly, the mean period of mechanical ventilation in group (B) was 68.31 hours, whilst it was 81.82 hours in group (A) (P= 0.035) (Table 4).

This study reported cardiopulmonary ultrasound parameters of the study group. TAPSE ranged between 0.86-2.47cm with Mean±SD 2.35±0.832cm. MAPSE ranged between 0.34-2.36cm with Mean±SD 1.34±0.655cm. Diameter of IVC ranged between 0.65-2.71cm with Mean±SD 1.62±0.642cm. In addition, LUSS ranged between 0-22 with Mean±SD 11.94±7.183, whilst EPSS ranged between 12.30-18.20cm with Mean±SD 15.19±1.875cm (Table 5).

Furthermore, no statistically significant variance was reported among the study groups, concerning white blood cells count, platelets, total bilirubin, serum creatinine, lactate, $PaCO_2$ and PaO_2/FiO_2. Mean PaO_2/FiO_2 in group A was 173.94, lower than that was reported in group (B) 184.61 (*P*= 0.102). In addition, serum lactate in group (A) reported a mean of 4.34mg/dl, compared to 4.63mg/dl in group B. No significant distinction was reported among the two study groups (Table 6).

Table 4: Comparison between the two groups regarding acute kidney injury, duration of mechanical ventilation and ICU stay:

Parameter	Group (A) (*n*= 54)	Group (B) (*n*= 54)	*P* Value
Acute kidney injury [*n* (%)]	15(27.7%)	10(18.5%)	0.15#
ICU stay (Days)	7.89±2.523	5.83±2.813	<0.001^
Duration of mechanical ventilation (Hrs.)	81.8±38.8	68.31±25.332	0.035^

Statistically significant at *P*<0.05; ^: Student t test; #: Chi-square test.

Table 5: Distribution of the study group as regard to patients' Cardiopulmonary Ultrasound parameters:

Parameter	Min.-Max.	Mean±SD
TAPSE mm	10-26	18.35±3.83
MAPSE mm	5-19	10.62±3.57
Diameter of IVC (cm)	0.65-2.71	1.62±0.64
LUSS	0-22	11.94±7.18
EPSS mm	4-15	8.23±1.87

TAPSE: Tricuspid annular plane systolic excursion; MAPSE: Mitral annular plane systolic excursion; IVC: Inferior vena cava; LUSS: Lung Ultrasound Severity Score; EPSS: E-Point Septal Separation.

Table 6: Laboratory parameters comparison between the two groups:

Parameter	Group (A) (*n*= 54)	Group (B) (*n*= 54)	*P* Value
WBCs	12.26±3.52	13.72±4.49	0.097
Platelets	108.46±27.27	110.96±26.57	0.630
Total Bilirubin	0.31±0.08	0.35±0.14	0.446
Serum Creatinine	2.62±0.72	1.87±0.60	0.064
Lactate	4.34±0.95	4.63±1.40	0.216
$PaCO_2$	38.76±4.42	35.63±3.98	0.086
PaO_2/FiO_2	173.94±31.63	184.61±35.48	0.102

Data are represented as means±SD; Using Student *t* test.

DISCUSSION

This study highlighted that the 72-hour mortality rate in group (A) was significantly higher than that reported in group B (*P*= 0.027). Regarding correlation between ultrasound variables, APACHE II, LUSS, HR and MAP to 72-hour mortality, this study found that Pearson's correlation coefficients between patient mortality and diameter of IVC, LUSS, EPSS, APACHE II score and serum lactate showed a strong positive correlation between these variables and mortality.

In consistent with the current results, Zou T. *et al.,* included a total of 181 shocked patients[1]. In univariate correlation analysis, the ultrasonic variables volume status, RV and LV systolic function, and LUSS score were evaluated. The results indicated that 27-day mortality was related with MAPSE, LUSS, abnormal volume status, and LV systolic dysfunction, respectively (*P*= 0.032, 0.001, 0.038, and 0.011). Consistent with the present findings, this research emphasized that the mortality rate after 28 days was 44.8 percent.

Moreover, Yin W. *et al.,* revealed that the most remarkable finding from the multivariate analysis of independent risk factors for 28-day mortality is that the mortality at 28 days was significantly linked with age, the LUSS, 0.011, 0.000, 0.048, 0.000, 0.008, 0.027, 0.031, 0.001, heart rate, lactate level, urine output, usage of vasoactive agents, and PaO_2/FiO_2. The LUSS, the APACHE II score, and the lactate level were shown to be independent risk factors for 28-day mortality in the multivariate analysis, which was limited to the variables that showed a significant variance in the univariate analysis. They also disclosed the 28-day death rate, which was 46.3%, for 175 patients that had a completed lung ultrasonography[4].

Conversely, Wang *et al.,* enrolled 128 patients who had experienced shock with acute pulmonary edema[8]. These individuals were randomly assigned to one of two groups: the sonography group, which received standard treatment in addition to cardiopulmonary sonography; or the control group, which solely received standard treatment. The ICU mortality rate did not vary significantly among the sonography and control groups (*P*= 0.470).

Furthermore, Li L. *et al.,* found that the twenty-eight-day mortality rate was not significantly different among both groups (ultrasound group and standard group) (50.6% vs. 60.0%)[9].

The present study demonstrated that period of mechanical ventilation in Group (B) was 68.31 hours, which was significantly lesser than that reported in group (A) 81.8 hours. There were statistically significant variances among groups where P= 0.035. In addition, this research stated that the duration of ICU stay in group (A) was 7.89 days while in group (B) was 5.83 days. There was statistically significant variance among groups where P below 0.001.

Consistent with our findings, Zou T. *et al.,* found that among the 181 individuals suffering from shock, 98.9 percent required mechanical ventilation, with a median duration of 68 hours on ventilator support[1]. In addition, they reported that the median duration of stay in ICU was 15 days. Moreover, Shokoohi H. *et al.,* demonstrated that hospital stay duration was five days, with IQR (2–11)[10]. Conversely, Li L. *et al.,* found that the duration of ICU stay revealed no significant variances among the groups[9].

In one study by Zou T. *et al.,* included 181 patients with shock, TAPSE was evaluated in 143 individuals (79 percent)[1]. The average TAPSE measurement was 1.76±0.53cm. Also, Sekiguchi H. *et al.,* reported that of the 30 cases undergoing resuscitation for severe sepsis or septic shock, the median maximal IVC diameter (mm) was 22 (IQR, 19–26), median minimal diameter (mm) was 18.5 (IQR, 10.5–20.5) mm[11]. In line with the study results, Li L. *et al.,* found that according to findings of focused cardiopulmonary ultrasonography, IVC diameter was 10-20mm in shocked patients[9].

According to results of the present research, no significant variance was reported between groups, concerning WBCs, platelets, total bilirubin, serum creatinine, and lactate. Mean $PaCO_2$ in group (A) was 38.76, while it was 35.63 in group (B). There was no statistically significant variance among groups. Similarly, mean PaO_2/FiO_2 was comparable in the two groups, with no significant difference. Mean PaO_2/FiO_2 in group (A) was 173.94, whilst it was 184.61 in group (B). Correspondingly, Wang et al., revealed that in sonography group, Lactate, mmol/L was 3.18±1.28. While in control group, Lactate, mmol/L was 3.39±1.37. There was no significant variance among the both groups (P= 0.368)[8] .

Furthermore, Sekiguchi *et al.,* reported that the median lactate levels were 2.7mmol/L (IQR 1.2–4.1mmol/L) in 30 cases undergoing resuscitation for severe sepsis or septic shock[11]. In addition, Zou T. *et al.,* found that the median lactate was 3.2 in 181 shocked patients, with interquartile range (IQR), 2.0-6.8[1].

Moreover, Yin *et al.,* revealed that of 175 shocked patients with a completed lung ultrasound exam, Lactate was 3.4, ranging from 2.0 to 6.8. They also reported that PaO_2/ FiO_2 was 185, ranging from 125 to 265[4].

In consistent with the current results, Zou *et al.,* found that in a total of 181 patients with shock, PaO_2/FiO_2 was 185, ranging from 44 to 620[1]. As well, Li L. *et al.,* (aimed to examine the impact of focused US on clinical results of septic shock), revealed that in cases of the ultrasound group and cases in the standard group respectively; the $PaCO_2$ was 34.0 and 39.0mmHg. PaO_2/FiO_2 was 190.0(126.7–241.3) and 170.0(115.00–225.8)[9]. They demonstrated there were no statistically significant variances among the both groups, concerning WBCs, Platelets, Total bilirubin, Lactate and Serum creatinine.

Additionally, Shokoohi *et al.,* who aimed to thoroughly evaluate the effects of an ultrasonography hypotension protocol on the diagnostic certainty, accuracy, treatment strategies, and resource use of emergency department in cases with undifferentiated hypotension. They showed that the median WBC count/mm^3 (IQR) was 9.26(6.5–13.89) and the median plasma lactate mmol/L (IQR) was 2.3(1.5–3.5)[10].

LIMITATIONS

Paucity of data limited the ability to enrich the discussion. Further randomized controlled studies are recommended to reach a more robust evidence.

CONCLUSION

This study revealed a significant decline in 72-hour mortality rate among ultrasound treated group in comparison with the control group. Integrated cardiopulmonary ultrasound resulted in shorter ICU stay and mechanical ventilation. Pearson's correlation coefficients between patient mortality and diameter of IVC, LUSS, EPSS, and APACHEII showed a strong positive correlation between these variables and mortality.

ABBREVIATIONS

TAPSE: Tricuspid annular plane systolic excursion; **MAPSE:** Mitral annular plane systolic excursion; **LUSS:** Lung Ultrasound Severity Score; **EPSS:** E-Point Septal Separation; **IVC:** Inferior vena cava; **MAP:** Mean arterial pressure; **EF:** Ejection Fraction; **CCUS:** Critical care ultrasound; **CPUS:** Cardiopulmonary Ultrasound; **APACHE II:** Acute Physiology And Chronic Health Evaluation.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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