Impact of shock multi-focused ultrasound diagnostic protocol as routine screening at early intensive care stay on morbidity and mortality rates in shocked critically ill patients: A randomized controlled trial

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Abstract

***Objective*: This study aimed to determine whether a shock multi-focused ultrasound protocol would improve mortality and morbidity rates, moreover, to evaluate the effect of ultrasound protocol in improving the secondary endpoint as the length of stay in shocked individuals attended to the intensive care unit (ICU).**

***Design*: A single-center randomized controlled trial.**

***Setting*: This study was done at Kasr Al-Ainy Hospital, Cairo University, Cairo, Egypt, during the period between March 2021 and April 2022.**

***Patients and participants*: Our prospective study was performed on 100 shocked individuals.**

***Interventions*: Patients were randomly distributed into 2 groups: Group A, which received conventional management and a routine evaluation with shock multi-focused ultrasound protocol, and Group B, as a control group, which solely provided conventional therapy to startled patients in the ICU in accordance with pre-established protocols.**

***Results and measurements*: This study revealed that a substantially critical reduction was present in vasopressor duration (p-value 0.03), vasopressor doses, and frequency of need for two vasopressors in Group A compared to Group B. Also, the mortality rate did not differ across the groups under study. However, there was a decrease in morbidity and other complications among Group A compared to Group B.**

***Conclusions*: We concluded that multi-focused ultrasound protocol should be seriously considered by physicians managing critically ill shocked patients as a tool to guide resuscitation, augment clinical evaluation, and improve quality of life by lowering morbidity rates, vasopressor doses, and duration.**

Key words: Shock, critically ill patients, multi-focused ultrasound, intensive care stay.

Introduction

Ultrasound has become an essential tool in the treatment of patients with shock, acute respiratory failure, or multi-organ failure. However, there is still a significant area of research in critical care ultrasound focused on producing scientifically-supported transformative changes. (1)

Due to the inherent limitations of a thorough physical examination of critically ill patients, imaging techniques such as computed tomography (CT) scans and chest and abdominal imaging are considered more dependable, practical, and effective in critical care situations. However, they are not without drawbacks, such as limited mobility and flexibility, as well as high costs, which can cause unnecessary delays in diagnosis and increase the risk of hypoxemia or refractory arterial hypotension during transport. (2)

Alternatively, a growingly popular and easily accessible approach that can be utilized at the bedside with portable equipment is ultrasonography. (3)

Recent studies have shown that multi-organ ultra-

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sound improves diagnostic precision, reduces resource usage, and helps guide therapeutic care for critically ill patients. (4) However, it's important to note that these previous publications lack randomized or controlled trial methodology.
Multi-organ ultrasonography is now widely utilized in the approach to shock patients in the emergency department and critical care setting, where it has been shown to be highly accurate in identifying the primary cause of shock. (5)
Studies that have quantified the clinical impact of ultrasound have shown that, depending on the clinical situation, ultrasound was used to adjust management strategies and revise diagnoses in 30 to 80 percent of cases. (6)
Most studies in this field have focused on single-organ scanning. However, in critical care medicine, a multi-organ strategy may be more appropriate for the initial evaluation of complex cases, as such cases often involve multiple organs. (7)
Patients with cardiopulmonary conditions, in particular, should be aware of this, as they have a wide range of potential diagnoses. In many cases, a combined heart and lung point-of-care ultrasound (POCUS) can help identify the cause of shock or significantly narrow down the range of potential diagnoses in these patients. (8)
Lower extremity vein POCUS, in addition to heart and lung POCUS, can effectively detect proximal deep venous thrombosis (DVT), which may result in pulmonary embolism, breath shortness, or cardiovascular crisis. (9)
In a randomized trial including emergency department patients with respiratory conditions, a multi-organ POCUS of the heart, lungs, and lower limb veins was discovered to be more effective than standard diagnostic tests alone for making a diagnosis within four hours. (10)
This study aimed to determine whether a shock multi-focused ultrasound protocol would improve mortality and morbidity rates, moreover, to evaluate the effect of ultrasound protocol in improving the secondary endpoint as the length of stay in shocked patients attended to the intensive care unit (ICU).

Methods

This prospective research was performed on 100 shocked individuals aged above 18 years who attended ICUs at Cairo University hospitals during the period between March 2021 and April 2022. This trial was conducted in accordance with the Declaration of Helsinki. All participants signed an informed written consent form. The study was done after being approved by the research ethics committee, Faculty of Medicine, Cairo University (Code: MD-154-2021).
Shock was described as a potentially fatal circulatory condition that results in insufficient oxygen supply to meet cellular metabolic requirements and oxygen uptake requirements, resulting in cellular and tissue hypoxia. (11)
Patients were randomly distributed into two groups by stratified cluster randomization according to comorbidities distribution into two groups as follows:

- Group A: Patients in this group were evaluated for the usage of ultrasound protocol.
- Group B: The control group, which the patients only in the ICU startled and were given conventional care in accordance with the recognized protocols.

Exclusion criteria: Patients with age <18 years, patients supported by an intra-aortic balloon pump or extracorporeal membrane oxygenation, and patients with a history of drug intoxication.

Operational design

All subjects in the study were subjected to clinical examination, including detailed history taking with special stress on age, gender, and presence of other comorbidities, especially diabetes mellitus (DM) and hypertension (HTN). We gathered clinical information, such as the sequential organ failure assessment (SOFA) score, acute physiology and chronic health evaluation (APACHE) II score at admission, the cause for admission to the ICU, and any pertinent physiologic data. Collected data also involved mean arterial pressure (MAP) at admission and also after 1-hour bundle of fluid resuscitation and added of vasopressors, urine output (UOP) ml/hour (by calculating the average amount of urine during an hour after the first 24 hours of care in ICU), and fluid balance after first 24 hours.
Our multi-focused ultrasound protocol included the following:

1. Focused cardiac ultrasonography (FOCUS).
   This was to assess a patient's level of global cardiac function, the size of their heart cavities, the existence of pericardial effusion, and their volume status. Finding the right ventricular diastolic dysfunction for cardiac tamponade in patients who have pericardial leakage was the next step. Based on a calculation of alterations in ventricular volume throughout systole and diastole, left ventricular contractility was assessed. For rapid assessment, qualitative assessment on visual inspection “eyeballing” was done to evaluate left ventricle function, then quantitative assessment of ejection fraction (EF) by “M mode”.

2. Inferior vena cava (IVC) evaluation.
   In individuals with spontaneous breathing, the caval index was utilized to assess the right atrial pressure. The formula for calculating the caval index was as follows: (Emax-Imax)/Emax (Emax=maximum diameter of IVC during expiration, Imax=minimum diameter of IVC during inspiration).
   IVC measures were utilized to calculate central venous pressure (CVP) because they were associated with CVP. Also, the distensibility index for passive mechanically ventilated patients was used for the evaluation of fluid state of patients.
3. Focused abdominal ultrasonography.
   It was applied to determine whether intraperitoneal free fluid was present.
4. Evaluation of abdominal aorta.
5. Thoracic ultrasonography.
   This was to assess the pulmonary edema presence, pneumothorax, and also to identify causes of shock by determining consolidation pneumonia in septic shock and pleural fluid as a complication for pump failure.
6. Ultrasonography imaging of lower limb veins.
   This was to evaluate the presence of DVT.

Endpoint data: We also collect data from both groups of study as the length of ICU stay, vasopressor dose after 3 hours from volume resuscitation, mechanical ventilation (MV) duration, need for dialysis, readmission within 30 days from admission, morbidity and mortality rates.

Sample size calculation

Based on the difference in mortality between cases, the sample size was calculated. The use of shock multi-focused ultrasound protocol during the first 5 days of ICU admission in critically ill shocked patients retrieved from previous research. (12) The sample size will be at least 49 cases for each group when using G*Power version 3.0.10 to determine sample size based on the predicted difference of 28 percent, 2-tailed test, error=0.05, and power 80.0 percent. (12)

Statistical analysis

Statistical analysis was conducted using version 27 of the SPSS program (Statistical Package for Social Science). Qualitative data were presented as frequencies and relative percentages. The chi-square test was used to assess the difference between qualitative variables. The independent t-test was used to compare quantitative variables between the two groups when the data were normally distributed. When data were not normally distributed, the Mann-Whitney test was used to determine the difference between quantitative variables in the two groups. Spearman's rank-order correlation was used to determine the strength and direction of a linear relationship between two non-normally distributed continuous variables and/or ordinal variables. A p-value <0.05 was considered statically significant.

Results

In this trial, 117 cases were evaluated for eligibility, but 14 did not meet the inclusion criteria. The remaining 103 cases were randomized into two groups. During the follow-up period, three patients were lost, leaving 100 patients for statistical analysis (**Figure 1**).

Statistically, there were no significant differences in the age or sex distribution across the groups of study (**Table 1**).

Table 2 shows that 28% of Group A cases had intraperitoneal free fluid (IPFF), 34% had pleural fluid, 16% had pre-exciting cardiac disease, 6% had pericardial effusion, 4% had cardiac tamponade, 14% was suspected pulmonary embolism (PE), 6% had deep vein thrombosis (DVT), 14% had pulmonary edema, 6% had pneumothorax, and 68% had pneumonia. The most frequent profile found by lung ultrasound was profile C (50%), followed by profile A (18%).

Table 3 and **Figure 2** indicate that there were no significant differences between the studied groups in terms of MAP on admission, UOP, fluid balance, and CVP. However, a significant increase in MAP after 1 hour and the frequency of patients with MAP>65 mmHg was observed in Group A compared to Group B. In terms of the type and dose of vasopressor, a significant increase in vasopressor dose and the frequency of patients receiving two types of vasopressors was observed in Group B compared to Group A.

Table 4 and **Figure 3** show the mortality rates and other morbidity and complication frequencies for both groups of the study. While there was a decrease in mortality rate in Group A compared to Group B, the difference was not statistically significant. However, there was a significant increase in the frequency of other morbidity and complications in Group B compared to Group A.

Table 5 and **Figure 4** reveal that statistically, there was a significant increase in the duration of vasopressor use among Group B cases compared to Group A cases (p-value 0.03). Additionally, the data indicate a decrease in length of stay, MV duration (p-value 0.07), need for dialysis, and readmission in Group A compared to Group B, although these differences were not statistically significant.

Table 6 and **Figure 5** demonstrate that the median APACHE and SOFA scores were significantly higher among cases with mortality compared to those who survived (26 vs 18) and (11 vs 9), respectively.

Discussion

According to the available evidence from studies, the use of POCUS has been shown to improve diagnostic confidence and increase diagnostic accuracy in identifying the type of shock and final diagnosis in patients with undifferentiated shock. POCUS has also been found to reduce the number of valid differential diagnoses, allowing for quicker and more accurate treatment decisions. (13)

In this randomized trial, we demonstrated that the use of critical care multi-focused ultrasound protocol in critically ill shocked patients significantly reduced ICU morbidity, such as acute kidney injury (AKI), and improved the second endpoint by showing a significantly decreased vasopressor duration.

Based on our study, there were no significant differences in age, sex distribution, or comorbidity frequency among the studied groups in terms of patient demographic and clinical profiles. Also, there were no significant differences observed in mechanical ventilation usage at admission between the studied groups.

Li et al. reported that 36 (73.5%) individuals in the integrated cardiopulmonary ultrasonography group and 34 (75.6%) individuals in the conventional group received assisted mechanical ventilation. Our study also showed that 37 (74%) patients in Group A and 38 (76%) patients in Group B received assisted mechanical ventilation, in accordance with Li et al.'s findings. (12)

In our study, a substantially considerable increase was observed in MAP after 1 hour, and the number of cases that had MAP>65 mmHg was higher in Group A than in Group B. This was consistent with a study by Ehab S. et al., which revealed a significant increase in MAP on admission. Systolic blood pressure (SBP) ranged between 40 and 80 mmHg, and diastolic blood pressure (DBP) ranged between 30 and 50 mmHg. At the end of resuscitation, it gradually increased with fluid therapy to 110-120 mmHg SBP and 80-90 mmHg DBP. (14)

Regarding type and dose of vasopressor, there was a significant increase statistically in the vasopressor dose, and the frequency of cases had 2 types of vasopressors among Group B compared to Group A.

According to our study, there were no substantial differences in fluid balance between the two groups. The multi-focused ultrasound group showed a slightly higher mean positive fluid balance (1.4 l vs 1.3 l, p=0.32), but this difference was statistically not significant. Similarly, there was no significant difference in the base deficit between the two groups (-7.8 vs -8.2, p=0.42).

This agreed with Li et al., who showed that the integrated cardiopulmonary ultrasonography group tended to have a higher fluid balance and fluid intake than the conventional group. Furthermore, there were no significant changes in the cumulative fluid infusion within 24 or 72 hours. (12)

In our study, although there was a decrease in mortality rate among Group A compared to Group B, the difference was not statistically significant. However, statistically, there was a significant increase in the frequency of other morbidities and complications among Group B compared to Group A.

The results of our study were consistent with previous studies by Talayeh Rezayat et al., who reported that there were no significant differences in mortality during hospitalization between the two groups, and no significant differences were seen in resource utilization, as evaluated by the number of echocardiograms, laboratory measures, or radiological tests needed between the two groups. (15)

Musikatavorn et al. also reported that there was no significant difference in 30-day overall mortality between the two groups (18.8% and 19.8% in the usual-care and ultrasound-guided fluid management strategy, respectively; p>0.05). (16)

Moreover, Li et al. reported that integrated cardiopulmonary ultrasonography had no significant effect on 28-day mortality in the integrated cardiopulmonary ultrasonography group vs the conventional group (50.6% vs 60.0%). (12)

Our study results differed from those reported by Yin W et al., who found that ICU mortality was lower in the critical care ultrasound-oriented treatment group compared to the standard care group (29.9% vs 45.7%, p=0.047). They also observed a higher 28-day risk of death after ICU admission in the standard care group (p=0.036). (17)

The differences in ICU mortality rate reduction in the present study from the previous studies were probably due to the quality of patients sharing in this study.

Our study demonstrated that there was a reduction in length of stay, mechanical ventilation duration, frequency of dialysis need, and readmission in Group A compared to Group B, although this difference was not statistically significant. However, there was a significant decrease in the duration of vasopressor use in Group A compared to Group B.

Our study's findings were consistent with those of Li et al., who reported a shorter duration of vasopressor support in the ultrasonography group. How-

ever, there were no differences in cumulative fluid infusion within 24 or 72 hours, lactate clearance, ICU stay, or duration of ventilation. (12)
Musikatavorn et al. reported that there was no significant difference in the length of hospital stay. However, the cumulative fluid amount given in 24 hours was significantly lower in the ultrasound-guided fluid management arm. (16)
The study by Talayeh Rezayat et al. found no significant difference in the length of stay or resource utilization between the two groups. However, rapid ultrasound for shock and hypotension (RUSH) subjects were more likely to have a lower stage of AKI by Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE) staging (p=0.019), and there were non-significant trends towards less total fluid administration. These findings were consistent with our results, which also showed a non-statistically significant decrease in the need for hemodialysis or ventilator days in the multi-focused ultrasound group. (15)
According to our study, there was a statistically significantly higher median APACHE score and SOFA score among cases with mortality than alive cases with p-value<0.01.
The two groups were also similar in prognostic scoring systems. The mean APACHE II score was 22 in Group A and 23 in Group B. Additionally, the mean SOFA score was 10.12±2.34 in the multi-focused ultrasound Group A and 10.16±2.34 in the usual care Group B.
This result was in accordance with Talayeh Rezayat et al., who showed that the mean APACHE IV score was 79.6 in the RUSH group vs 80.9 in the control group (p=0.830). (15)
Moreover, this was in accordance with Hai and Viet Hoa, who showed that the APACHE II sensitivity was 84.9% and specificity of 67.7%, SOFA score sensitivity was 76.7% and specificity of 65.3% for mortality prediction and was the independent mortality predictor in patients with sepsis. (18)
Also, Gursel G. and Demirtas S. showed that the mortality prediction was excellent for APACHE II (p=0.001) and acceptable for SOFA (p=0.005) scores. Only APACHE II >16 was an independent predictor of mortality (p=0.019) in the logistic regression analysis. (19)
In our study, there was a non-statistically significant correlation between length of stay and APACHE score and SOFA score.
This was also agreed with Naved et al., who showed that in the lowest score category 3-10, 27 out of 30 patients (90%) were discharged, and only 3 (10%) died. Out of those 39 patients whose APACHE-II score was found in high category 31-40, 33 (84.6%) deaths were observed. This revealed that there might be more chances of death in case of a high APACHE-II score (p=0.001). Moreover, this study showed that there was an insignificant but inverse correlation (r=-0.084, p<0.183) observed between the APACHE-II score and the length of ICU stay. (20)
Our study showed that there was a statistically significant difference detected between hypovolemic shock and the reduction of mortality rates in comparison to other types of shock.
This result was in accordance with Gitz et al., who showed that patients with septic and cardiogenic had a higher mortality rate as compared to the reference (non-septic shock) within 0 to 7 days. (21)

Limitations

Our study had limitations because we had a practical deadline of 12 months to complete data collection, therefore, we lacked an adequate sample size to discover statistically significant variations in mortality rates.
Also, because specific demographics, such as children or pregnant patients, were not included in our study, it was possible that these patients were not accurately represented.
In this study, the physicians were not blinded, which may have led to bias. Since there was additional attention on the study group than the control group, this might lead to more focus on the patient and a better result in the study group.
Additional confounding factors that were not necessarily connected to the admission diagnosis could alter the outcomes when patients stayed longer in the ICU (late-onset, ventilator-associated pneumonia). Although mortality was similar between the two groups, it should be emphasized that future research with bigger patient populations and shorter MV durations than those in the POCUS group may reveal a decline in death from MV problems.

Conclusions

In the view of this study, we concluded that multi-focused ultrasound should be seriously considered by physicians managing critically ill shocked patients as a tool to guide resuscitation, augment clinical evaluation, and improve quality of life by lowering complications, vasopressors doses, and vasopressor duration in the intensive care units.

Table 1. Demographic and clinical data analysis in both groups

Variable		Group A (n=50)		Group B (n=50)		t	p-value
Age (years)	Mean±SD Range	57.36±16.99 18-85		60.52±14.59 18-83		0.99	0.32 (NS)
Variable		n	%	n	%	χ^2	p-value
Sex	Female Male	20 30	40 60	23 27	46 54	0.37	0.55 (NS)

Legend: SD=stander deviation; t=independent t-test; χ^2=chi square test; NS=non-significant (p>0.05).

Table 2. Multi-focused ultrasound protocol finding

Variable		Group A (n=50)	
		n	%
IPFF	No	36	72
	Yes	14	28
Pleural fluid	No	33	66
	Yes	17	34
Preexisting cardiac disease	No	42	84
	LV hypertrophy	2	4
	LV and LA dilation	3	6
	Right side dilation and hypertrophy	3	6
Pericardial effusion	No	47	94
	Yes	3	6
Cardiac tamponade	No	48	96
	Yes	2	4
Suspected PE	No	43	86
	Yes	7	14
DVT	No	47	94
	Yes	3	6
AAA	No	50	100
Lung ultrasound	A profile	9	18
	A profile and pleural effusion	2	4
	B profile	3	6
	B profile and pleural effusion	7	14
	C profile	25	50
	C profile and pleural effusion	2	4
	Lung point	2	4
Pulmonary edema	No	43	86
	Yes	7	14
Pneumothorax	No	47	94
	Yes	3	6
Pneumonia	No	16	32
	Yes	34	68
Volume state	Normovolemia	14	28
	Hypovolemia	26	52
	Hypervolemia	10	20
IVC	Spontaneous breath	27	54
	Passive MV	23	46
IVC diameter (cm)	Mean±SD	1.83±0.55	

Legend: IPFF=intraperitoneal free fluid; PE=pulmonary embolism; DVT=deep vein thrombosis; AAA=abdominal aortic aneurysm; IVC=inferior vena cava; LV=left ventricle; LA=left atrium; MV=mechanical ventilation; SD=standard deviation.

Table 3. Analysis of ICU data among the studied groups

Variable		Group A (n=50)	Group B (n=50)	Test	p-value
MAP admission (mmHg)	Mean±SD	52.39±7.81	53.91±8.03	0.78^	0.44 (NS)
MAP after 1h (mmHg)	Mean±SD	75.56±12.93	69.56±12.34	2.37^	0.02*
	<65 mmHg, n (%) ≥65 mmHg, n (%)	8 (16%) 42 (84%)	17 (34%) 33 (66%)	4.32$	0.03*
UOP (ml/hr)	Median (range)	75 (0-120)	80 (0-100)	0.34#	0.73 (NS)
Fluid balance (24hr)	Median (range)	1400 (-1700 - 4600)	1300 (-1550 - 4750)	0.99#	0.32 (NS)
CVP	Median (range)	7 (0-30)	9.5 (0-35)	0.47#	0.64 (NS)
Vasopressors	NA, n (%) NA and adrenaline, n (%)	47 (94%) 3 (6%)	40 (80%) 10 (20%)	4.33$	0.04*
Noradrenaline dose (mcg/kg/min)	Median (range)	0.51 (0.12-1.4)	0.62 (0.09-1.60)	2.13#	0.03*
Adrenaline dose (mcg/kg/min)	Median (range)	0 (0-0.78)	1 (0-1.5)	1.98#	0.04*

Legend: ICU=intensive care unit; MAP=mean arterial pressure; UOP=urine output; CVP=central venous pressure; SD=standard deviation; NA=noradrenaline; NS=nonsignificant (p>0.05).
^Independent t-test; $chi square test; #Mann-Whitney test, *significant (p<0.05).

Table 4. Mortality among the studied groups

Variable		Group A (n=50)		Group B (n=50)		χ^2	p-value
		n	%	n	%		
Mortality	No Yes	26 24	52 48	23 27	46 54	0.36	0.55 (NS)

Legend: χ^2=chi square test; NS=non-significant (p>0.05).

Table 5. Secondary endpoint among the studied groups

Variable		Group A (n=50)	Group B (n=50)	Test	p-value
Length of stay (day)	Median (range)	7 (2-28)	9 (3-23)	0.16#	0.88 (NS)
MV duration (day)	Median (range)	5 (0-24)	7 (0-23)	1.83#	0.07 (NS)
Vasopressor duration (day)	Median (range)	5 (2-21)	6 (2-21)	2.15#	0.03*
Need for dialysis	No, n (%) Yes, n (%)	40 (80%) 10 (20%)	38 (76%) 12 (24%)	0.233$	0.81 (NS)
Readmission within 30 days	No, n (%) Yes, n (%)	46 (92%) 4 (8%)	44 (88%) 6 (12%)	0.444$	0.51 (NS)

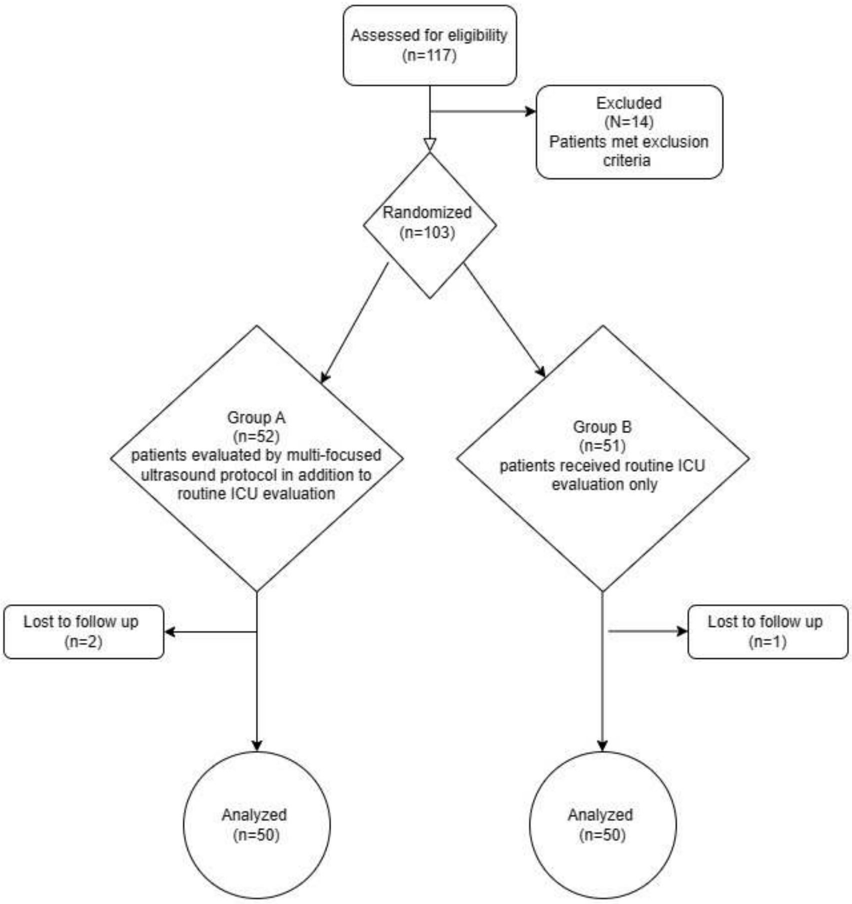
Legend: MV=mechanical ventilation; NS=non-significant (p>0.05).
#Mann-Whitney test; $Chi square test; *Significant (p<0.05).

Table 6. Correlation between SOFA and APACHE scores and mortality

	Mortality		Mann-Whitney U test
	No (n=49)	Yes (n=51)	
APACHE score, median (min-max)	18 (8-32)	26 (12-39)	z=5.03 (p<0.001)
SOFA score, median (min-max)	9 (6-13)	11 (7-17)	z=4.02 (p<0.001)

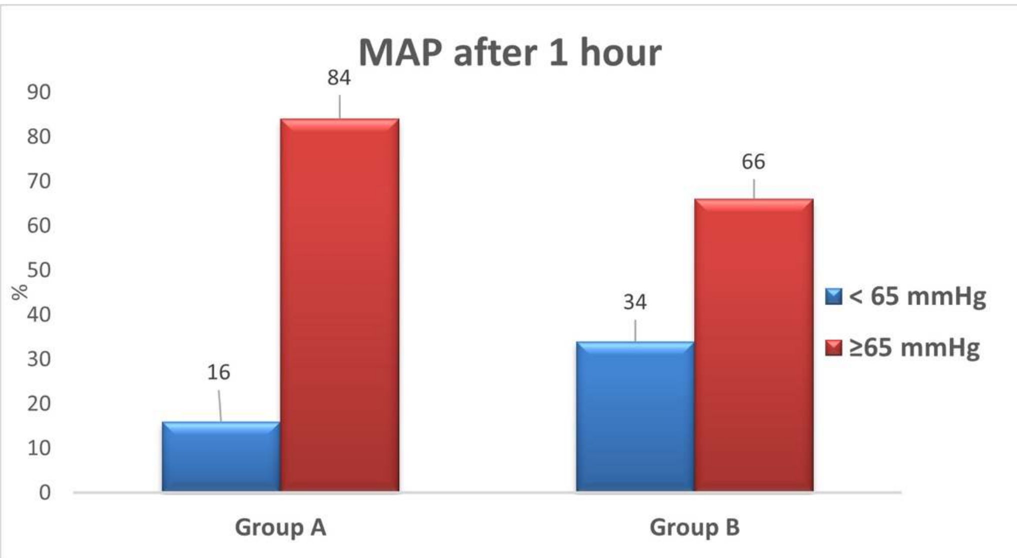
Legend: SOFA=sequential organ failure assessment; APACHE=acute physiology and chronic health evaluation.

Figure 1. Flowchart of the studied patients



Legend: ICU=intensive care unit.

Figure 2. MAP after 1 hour among the studied groups



Legend: MAP=mean arterial pressure.

Figure 3. The mortality rate among the studied groups

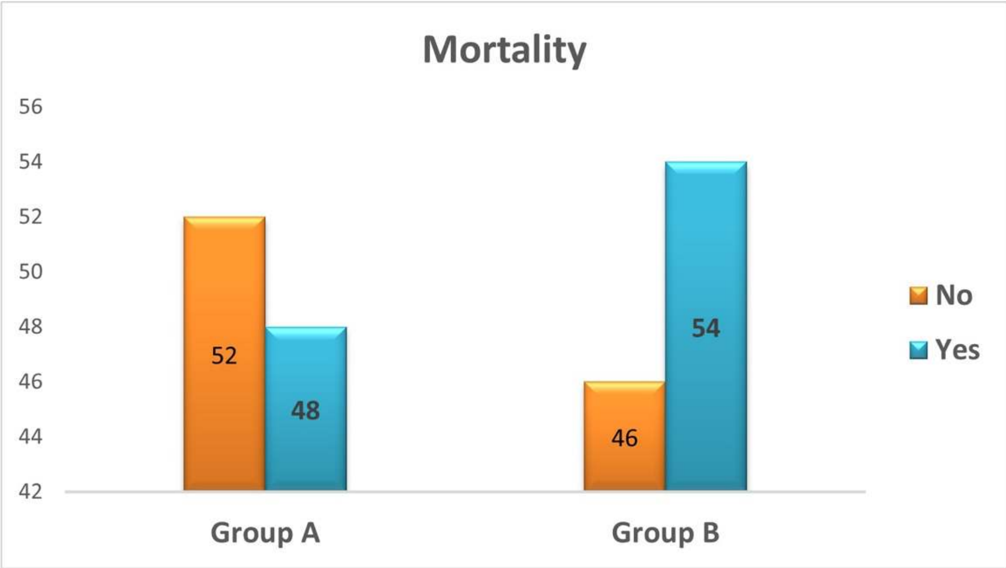
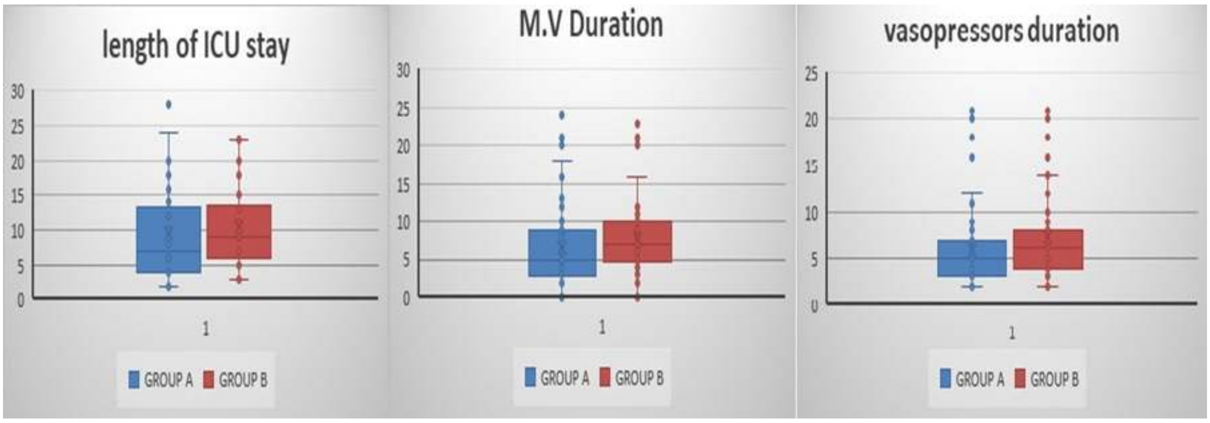
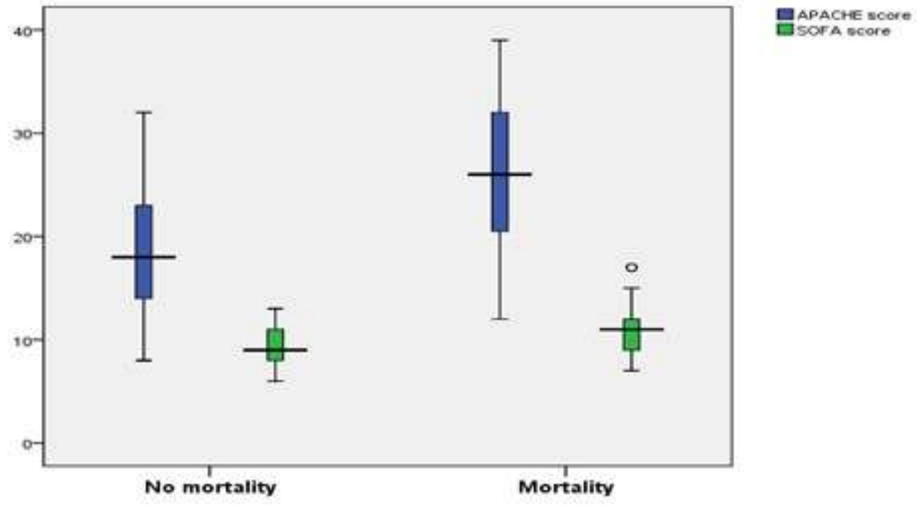


Figure 4. Length of ICU stay, MV duration, and vasopressor duration among the studied groups



Legend: ICU=intensive care unit; MV=mechanical ventilation.

Figure 5. Correlation between SOFA and APACHE scores and mortality



Legend: SOFA=sequential organ failure assessment; APACHE=acute physiology and chronic health evaluation.

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