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ORIGINAL RESEARCH INTENSIVE CARE

Echocardiography-guided hemodynamic management of severe sepsis and septic shock in adults: a randomized controlled trial

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Abstract

Background: Echocardiography (ECHO) is used to guide septic shock resuscitation, but without evidence for efficacy. Therefore, we compared the outcome of early goal-directed therapy (EGDT) and ECHO-guided management of hemodynamics in severe sepsis and septic shock.

Methodology: This was a single center, randomized controlled trial conducted on 100 adult patients with severe sepsis or septic shock. Patients were assessed and treated with either EGDT protocol (Group I - EGDT group) or ECHO-guided resuscitation protocol (Group II - ECHO group).

Results: Only 87 patients (45 in Group I and 42 in Group II) were analyzed. There was a significant increase of mean norepinephrine and dobutamine use and a significant decrease in total fluids needed in the first 24 h, time to normalization, time to weaning of vasopressors, total mechanical ventilation (MV) days, MV free days and ICU and hospital stay in ECHO group. At 30 days, the mortality rate in EGDT group was 35.6% which was significantly higher compared to 14.3% in the ECHO group. At 90 days, the overall mortality was significantly higher in EGDT group compared to ECHO group (40.0% vs 16.7% respectively). Hazardous ratio of mortality was 1.630 [95% confidence interval (CI): 1.123 - 2.366] and 1.653 (95% CI: 1.137 - 2.404) at 30 and 90 days respectively in EGDT group compared to ECHO group.

Conclusions: In severe sepsis and septic shock, ECHO-guided management of hemodynamics resulted in a decrease in mortality, lower total fluid intake, higher vasopressor and inotrope support, earlier weaning of vasopressors; and reduced mechanical ventilation days, as well as ICU and hospital stay.

Keywords: Echocardiography; EGDT; Severe sepsis; Septic Shock; Adults

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1. Introduction

Severe sepsis and septic shock are common in critically ill patients and are on top of the causes of mortality in intensive care units (ICU).[1] Vasodilation, increased permeability, hypovolemia, and ventricular dysfunction are the main findings in septic shock. [2]

A paradigm of "early goal-directed therapy" (EGDT) has been dominated in sepsis resuscitation for about fifteen years, based on the results of a single-center,

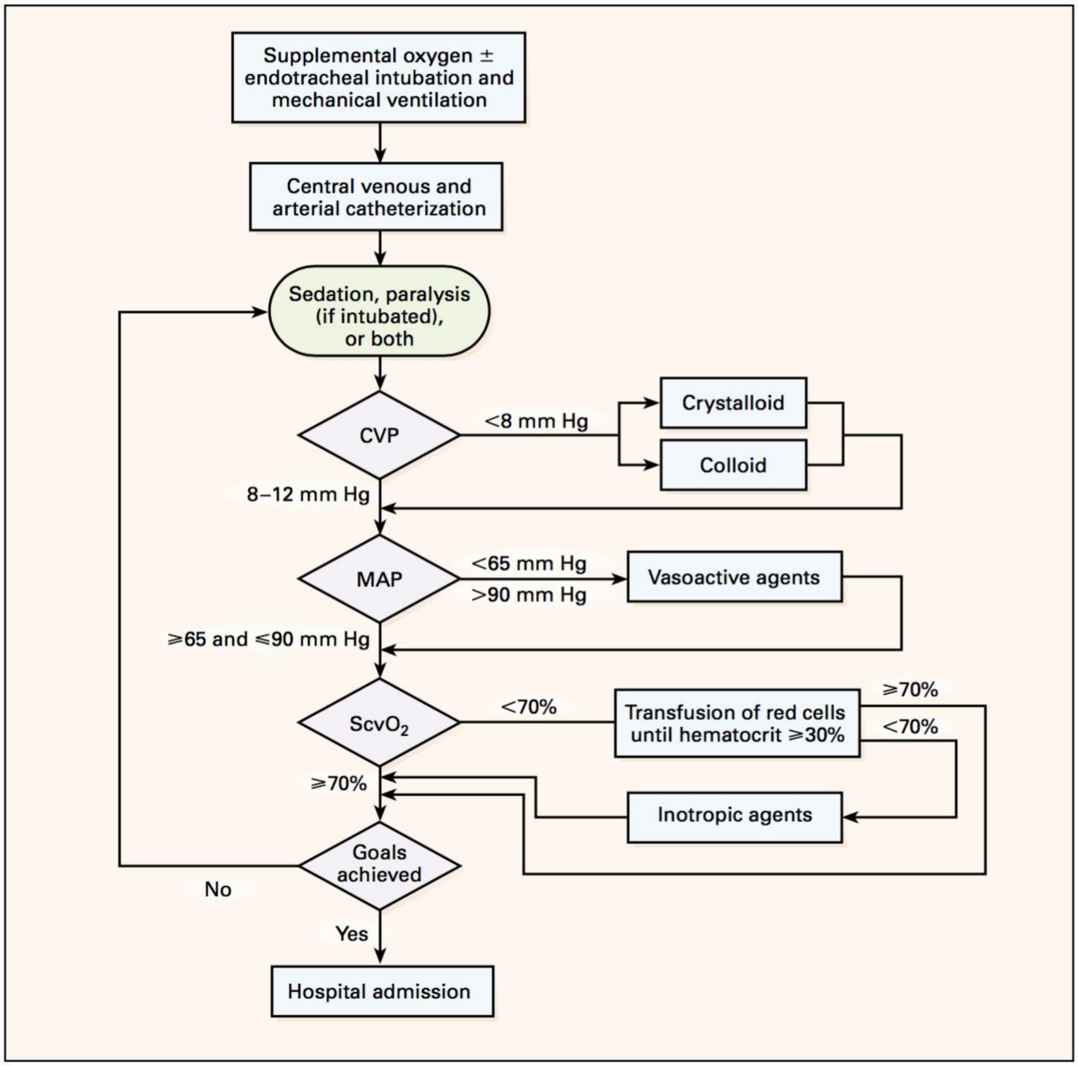

Figure 1: Early goal directed therapy (EGDT) protocol in severe sepsis /septic shock

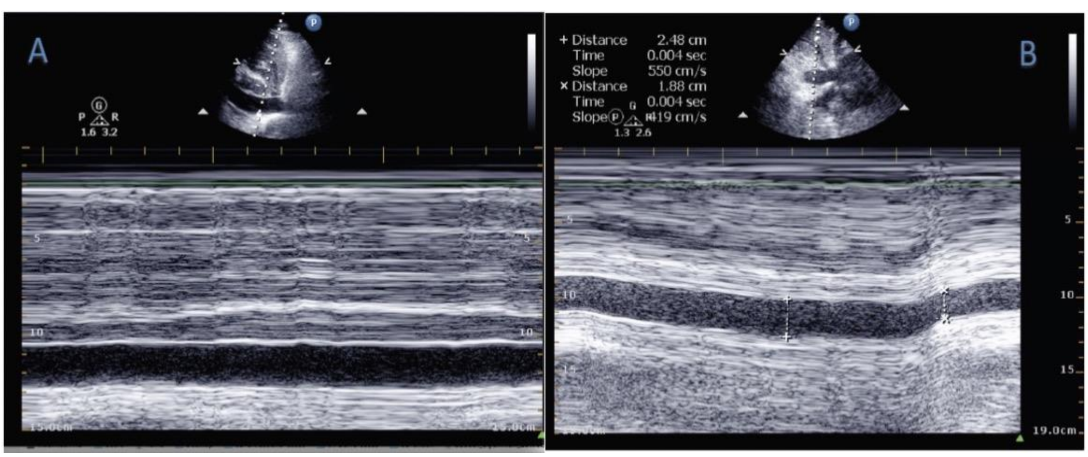

Figure 2: IVC Collapsibility is showing non-fluid responder in (a) compared to potential fluid responder in (b), velocity time integral (VTI) variation on the left ventricular outflow tract (LVOT) variability is showing a fluid responsive patient

randomized, "usual care" controlled study.[3] EGDT was not, however, studied in large, multinational, multicenter trials; even the patients received more intensive fluid in the "usual care" group than in the control group in the first study.[4-7]

Due to the failure of several negative randomized controlled trials to obtain similar benefits as the initial trial, the ideal approach to resuscitate patients with septic shock is still uncertain. Research is ongoing to find an optimal balance between administering large volumes of intravenous fluids that can have deleterious effects, or small volumes of fluids that fail to support adequate organ perfusion.[8]

Previously, the invasive assessment of hemodynamic parameters using central venous catheters and/or pulmonary artery catheters allowed clinicians to define cardiovascular physiology and dominated fluid management for many years.[9] However, the use of such techniques has significantly been decreased due to risks associated with their use. In addition, their "static" variable outcomes poorly predicted fluid responsiveness, and prospective studies showed no benefit from their routine use.[10-15]

Nowadays, critical care physicians are increasingly employing the echocardiography (ECHO) in the non-invasive assessment of hemodynamic parameters during hemodynamic instability. Many clinicians advocate the use of ECHO as a vital tool in the management of the critically ill patient.[16, 17]

Despite the adequacy of focused ECHO in the early stages of septic shock, a comprehensive systemic ECHO assessment of cardiac output, left and right ventricular systolic functions, volume status and filling pressure is crucial to provide a comprehensive hemodynamic management. Unfortunately, outcome studies on the utilization of ECHO in septic shock are not adequate and are therefore strongly required.[18]

This study compared the outcome between EGDT and ECHO-guided management of hemodynamics in severe sepsis and septic shock in adult patients.

2. Methodology

This randomized controlled clinical trial was conducted from March 2015 to May 2016 at surgical ICU, after ethics committee approval. Informed written consent was obtained from each patient or the next of kin. All data of patients were confidential with secret codes and saved in private file of each patient. All given data were used for the current medical research only.

The target population included 100 patients aged 18 to 60 y, admitted or planned for admission to ICU for an episode of severe sepsis and septic shock. Severe sepsis and septic shock was defined by the American College of Chest Physicians/Society of Critical Care Medicine consensus criteria.[19]. Patients met criteria for inclusion if they had; (1) a suspected infection, (2) two or more systemic inflammatory response syndrome criteria, and (3) either: (a) had severe sepsis (end-organ dysfunction) or (b) had septic shock (a systolic blood pressure less than 90 mmHg despite an intravenous fluid challenge of at least 20 ml/kg with evidence of organ dysfunction or hyperlactatemia).

Exclusion criteria were patient refusal to be included, known history of any cardiac disease, acute coronary syndrome, cardiac dysrhythmias (as a primary diagnosis), acute pulmonary edema, status asthmaticus, body mass index > 35 kg/m^2, severe respiratory disorders or high PEEP requirements on mechanical ventilation (MV), liver insufficiency, multi-organ system failure, contraindication to central venous catheterization, active gastrointestinal hemorrhage, and/or do-not-resuscitate status.

After stabilization of the airway and breathing, standard continuous monitoring of ECG, respiratory rate (RR), oxygen saturation and invasive arterial blood pressure was done. Then venous access was achieved and fluid resuscitation and empirical antibiotics were started.

Patients were randomly allocated into two equal groups (n = 50). Randomization was accomplished by a volunteer, not participating in the study, by computer generated sequence through sealed opaque envelopes.

2.1. Group I (EGDT group):

In this group the 'surviving sepsis campaign' dependent resuscitation protocol was applied, and targeted all of the following as a part of a stepwise treatment protocol;
500-ml bolus of crystalloid was given every 30 min to achieve a central venous pressure (CVP) of 8 to 12 mmHg. If mean arterial pressure (MAP) was less than 65 mmHg, vasopressors (noradrenaline 0.05-0.3 µg/kg/min) were given to maintain a MAP of at least 65 mmHg. If the central venous oxygen saturation ($ScvO_2$) was less than 70%, red cells were transfused to achieve a hematocrit of at least 30%. After the CVP, MAP, and hematocrit were thus optimized, if the $ScvO_2$ was less than 70%, Dobutamine administration was started at a dose of 2.5 µg/kg/min, a dose that was increased by 2.5 µg/kg/min every 30 min until the $ScvO_2$ was 70% or higher or until a maximal dose of 20 µg/kg/min was reached. Dobutamine was decreased in dose or discontinued if the heart rate (HR) was above 120 beats/min (Figure 1).[3]

2.2. Group II (ECHO group):

In this group a transthoracic bedside focused echocardiographic assessment of the patient was done, as a baseline ECHO in a five-step approach to monitor hemodynamics using Philips (CX50 – Extreme edition) machine with S5-1 ECHO probe.

Step 1: Starting point was to detect potential signs of pre-existing chronic cardiac dysfunction that needed a full formal ECHO study and exclude the patient from this study, as these findings can mislead interpretation of subsequent findings (i.e. primary cardiogenic cause of shock, instead of sepsis, LV or LA significant dilatation, and LV marked hypertrophy are signs or chronic volume/pressure overload; RA significant dilatation, RV dilatation and hypertrophy have the same meaning for right-sideed chronic disease (isolated RV dilatation can vice versa be a sign of acute RV dysfunction).

Step 2: LV/RV contractility assessment by eyeballing categorizing into hyperdynamic, good and poor function with

Step 3: LVOT VTI assessment by Echo Doppler, a low output state can then be ascribed to sepsis-related LV systolic dysfunction (± RV dysfunction) or isolated RV dysfunction and treated with inotropic support ± vasopressors (depending on MAP after inotropic support).

Low output with evidence of normal biventricular systolic function should prompt investigation of fluid responsiveness.

(Step 4): Fluid responsiveness assessed by 3 parameters (A) IVC Collapsibility (Figure 2A, Figure 2B) (B) passive leg raising test and (C) velocity time integral (VTI) variation on the left ventricular outflow tract (LVOT). If the patient was a fluid responder, he received infusion of 500 ml of crystalloids. When inadequacy of global perfusion and/or hypotension was associated with a non-low output state, persistent preload defect should be investigated (again step 4) and if detected, must be corrected.

If this was not the case, an exclusion diagnosis of vasodilatation was made **(Step 5)**, and systemic arterial tone corrected with upward titration of vasopressors. Whenever this was done, LV systolic/diastolic functions should subsequently be re-assessed, as normalization of LV afterload can unmask sepsis related myocardial dysfunction. Diastolic function was assessed using spectral doppler on mitral inflow and using tissue doppler of the septal mitral annulus in apical four chamber view to measure e' and a' velocities (Figure 3).

2.3. Echocardiographic parameters:

were repeated before each change in the management of fluids, vasopressors or inotropes, as well as just before discharge from the ICU.

IVC Collapsibility diameter less than 2 cm and index more than 50% indicates fluid responsiveness in spontaneously breathing patients. IVC distensibility index > 18% indicates fluid responsiveness in MV patients. Passive leg raising test > 10% increase in SV indicates fluid responsiveness (Figure 4).

2.4. In both groups:

The source of sepsis was early treated or eradicated according to the situation. The time of the study was the first 24 h.

2.5. Measurements

Demographic characteristics and clinical parameters (e.g., HR, RR, core temperature, invasive MAP, CVP and urine output) were recorded. Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated on 24 hours of study enrolment in both groups. Laboratory parameters (e.g., complete blood count, serum urea and creatinine) were noted daily for three days to be incorporated in the severity scoring system. Also, central venous saturation, arterial lactate level and arterial blood gases were recorded. Total fluid requirements in first 24 h from initiation of therapy, vasopressors and inotropic drugs requirements in first 24 h, time till normalization of the tissue perfusion indicators, time till weaning of vasopressors and inotropic drugs, MV and ventilator-free days, ICU length of stay, mortality at 30 and 90 days of admission were recorded.

The primary outcome was mortality at 30 days and the secondary outcomes were mortality at 90 days, the total fluid intake, MV-free days and duration of ICU and hospital stay.

2.6. Statistical analysis

The sample size calculation was performed using G*Power 3.1.9.2. on the following considerations: 0.05 α error and 80% power of the study and group ratio 1:1 to demonstrate a 25% decrease (expected) in mortality (the primary outcome) with ECHO-guided compared to EGDT management of hemodynamics (35% according to a previous study. [20]). To overcome dropout, 7 cases were added to each group. Therefore, 50 patients were recruited in each group.

The collected data were organized, tabulated and statistically analyzed using SPSS version 20 (IBM® SPSS® Inc., Chicago, Illinois, USA). All data were assessed for normal distribution using Shapiro-Wilks test. Quantitative parametric data were presented as mean ± standard deviation and compared by unpaired Student's t–test. Quantitative non-parametric data were presented as median and interquartile range and compared by Mann-Whitney U test. Qualitative variables were expressed as frequency and percent and

Table 1: Patients' characteristic of the studied patients

Parameters		Group I (EGDT) (n=45)	Group II (ECHO) (n=42)	Test	p-value
Age (y)	(Mean ± SD)	44.44 ± 7.65	42.33 ± 8.96	T = 0.18	0.24
Sex	Male	23 (51.1)	24 (57.1)	X^2 =0.31	0.57
	Female	22 (48.9)	18 (42.9)		
BMI (kg/m^2) (Mean ± SD)		27.93 ± 3.04	27.90 ± 2.73	T = 0.04	0.96
BSA (m^2) (Mean ± SD)		1.90 ± 0.14	1.90 ± 0.13	T = 0.14	0.88
Source of sepsis	Respiratory tract	19 (42.2)	16 (38.1)	X^2 = 2.98	0.81
	Soft tissue	11 (24.4)	7 (16.7)		
	Blood	5 (11.1)	6 (14.3)		
	Urinary tract	4 (8.9)	6 (14.3)		
	Abdomen	4 (8.9)	5 (11.9)		
	Endocarditis	0 (0)	1 (2.4)		
	Unknown	2 (4.4)	1 (2.4)		
Type of organism	Gram positive	18 (40.0)	14 (33.3)	X^2 = 0.59	0.74
	Gram negative	16 (35.6)	15 (35.7)		
	Mixed	11 (24.4)	13 (31)		
Need for mechanical ventilation		41 (91.1)	38 (90.5)	FE: ---	0.918
APACHE II score (Mean ± SD)		24.76 ± 4.26	23.95 ± 3.45	T = 0.79	0.42

Data given as n (%) unless described in the table. EGDT: early goal directed therapy group; Echo: echocardiography group; BMI: body mass index; BSA: body surface area, T: Student's t test, X2: Chi-square, FE: Fisher's Exact test

were compared by Chi-square (X^2) test. A p-value < 0.05 was considered statistically significant.

Registration: Pan African Clinical Trials Registry, PACTR201902680224481, Registered 6/12/2018; https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=5786

3. Results

In this study, only 87 patients with severe sepsis/septic shock were analyzed; 45 patients in Group I (5 cases were withdrawn) and 42 patients in Group II (8 cases dropped out; 1 case with poor window, 4 cases with chronic cardiac dysfunction and 3 cases were withdrawn). (Figure 5).

Both groups in our study were matched in the baseline characteristics (age, sex, BMI and body surface area (BSA). The source of sepsis, type of organism, need for mechanical ventilation and APACHE II score were comparable between both groups (Table 1).

BSA was calculated by Mosteller Formula (BSA=0.01667x W0.5xH0.5). MAP showed significant increase in ECHO group compared to EGDT group at 6 and 12 h. In each group, there was significant increase in MAP at 6, 12 and 24 h compared to baseline values. HR showed significant decrease in ECHO group compared to EGDT group at 6, 12 and 24 h. In addition, there was significant progressive decrease in each group at 6, 12, and 24 h compared baseline values. Core body temperature showed no significant differences at baseline and at 6, 12 and 24 h between both groups (Table 2).

CVP was significantly lower in EGDT group compared to ECHO group at baseline. Then, values in EGDT progressively increased with time, while values in ECHO increased at 6 h, then decreased nearly to baseline values at 12 h and progressively decreased at 24 h. The difference between both groups was non-significant at 6 h, while at 12 and 24 h, there was significant decrease in ECHO group compared to EGDT group (Table 2).

ScvO2 showed significant increase in ECHO group compared to EGDT group at 6, 12 and 24 h. Lactate concentration showed significant decrease at 24 h in ECHO group compared to EGDT group. pH was significantly higher in ECHO group at 12 and 24 h. Urine output showed no significant difference between both groups at the first 6 h. However, urine output was significantly increased in ECHO group compared to EGDT group at 12 and 24 h (Table 2).

Table 2: Vital signs, central venous pressure, central venous oxygen saturation, lactate concentration, pH and urine output of the studied patients

Parameters	Time to record	Group I (EGDT) (n=45)	Group II (ECHO) (n=42)	T	p-value
Mean arterial pressure (mmHg)	Baseline	58.31 ± 6.29	56.57 ± 7.49	1.17	0.24
	At 6 hours	66.31 ± 4.32	74.98 ± 9.24	5.65	<0.001
	At 12 hours	67.91 ± 3.30	81.43 ± 12.06	7.23	<0.001
	At 24 hours	69.51 ± 2.46	70.05 ± 2.09	1.09	0.27
Heart rate (beats/min)	Baseline	119.78 ± 13.23	113.62 ± 16.04	1.97	0.52
	At 6 hours	116.02 ± 10.96	100.05 ± 9.77	7.15	<0.001
	At 12 hours	107.47 ± 10.63	95.31 ± 7.8	6.04	<0.001
	At 24 hours	106.82 ± 22.92	84.90 ± 7.85	5.88	<0.001
Core body temperature (°C)	Baseline	37.98 ± 1.34	38.16 ± 1.25	0.62	0.53
	At 6 hours	37.54 ± 1.08	37.43 ± 1.24	0.41	0.67
	At 12 hours	37.46 ± 0.58	37.19 ± 0.74	1.92	0.06
	At 24 hours	37.47 ± 0.62	37.24 ± 0.65	1.65	0.10
Central venous pressure (mmHg)	Baseline	6.89 ± 2.87	10.38 ± 4.03	4.67	<0.001
	At 6 hours	11.2 ± 2.39	11.19 ± 3.44	0.02	0.98
	At 12 hours	11.73 ± 1.94	10.38 ± 3.13	2.43	0.017
	At 24 hours	12.07 ± 1.87	9.6 ± 2.84	4.81	<0.001
Central venous oxygen saturation (%)	Baseline	61.2 ± 7.43	65.9 ± 3.47	1.57	0.508
	At 6 hours	65.82 ± 5.82	69.37 ± 5.36	3.81	0.004
	At 12 hours	65.82 ± 5.82	70.79 ± 4.00	2.79	0.006
	At 24 hours	68.36 ± 4.97	71.24 ± 4.62	2.69	0.006
Lactate concentration (mmol/L)	Baseline	6.02 ± 1.51	6.38 ± 1.62	1.07	0.28
	At 6 hours	5.03 ± 1.27	5.26 ± 1.68	0.71	0.47
	At 12 hours	4.54 ± 1.42	4.08 ± 1.24	1.58	0.12
	At 24 hours	3.74 ± 2.42	2.32 ± 0.61	3.68	<0.001
pH	Baseline	7.16 ± 0.12	7.2 ± 0.09	1.95	0.54
	At 12 hours	7.23 ± 0.09	7.28 ± 0.07	1.99	0.049
	At 24 hours	7.27 ± 0.08	7.36 ± 0.06	5.46	<0.001
Urine output (mL)	At 6 hours	216.24 ± 140.13	254.33 ± 190.46	1.06	0.28
	At 12 hours	414.67 ± 284.33	622.74 ± 189.19	3.98	<0.001
	First day	751.31 ± 485.13	1070.55 ± 338.23	3.71	<0.001

Data are presented as mean ± SD, T: Student's t test

There was a significant increase in mean norepinephrine and dobutamine doses required in ECHO group compared to EGDT group. In addition, there was significant decrease in total fluids in the first 24 hours, time to normalization, time to weaning of vasopressors, total MV days, MV free days and the duration of ICU and hospital stay in ECHO group compared to EGDT group (Table 3).

At 30 days, mortality rate in EGDT group was 35.6% (16 patients), which was significantly higher compared to 14.3% (6 patients) in ECHO group. At 90 days, the overall mortality was significantly higher in EGDT group compared to ECHO group, e.g., 18 (40.0% vs 7 (16.7%) patients respectively (Table 3).

Hazardous ratio of mortality was 1.630 (95% confidence interval (CI): 1.123 - 2.366) and 1.653 (95%

Table 3: Outcomes of the studied patients

Parameter	Group I (EGDT) (n=45)	Group II (ECHO) (n=42)	Test	p-value
Fluids in the first 24 hours (mL)	3635.56 ± 973.32	2564.29 ± 927.58	T = 5.24	<0.001
Norepinephrine dose (µg/kg/h)	0.1 (0.05 - 0.2)	0.3 (0.2 - 0.34)	U = 308.5	<0.001
Dobutamine dose (µg/kg/h)	2.50 (0 - 7.5)	7.50 (5 – 10)	U = 538.0	<0.001
Time to normalization	36 (27.2 - 66.8)	12 (7 – 16)	U = 114.5	<0.001
Time to weaning vasopressors (h)	48 (24 – 72)	24 (12 – 24)	U = 231.0	<0.001
Total MV days	10 (6 – 12)	7 (5 – 8)	U = 501.0	<0.001
MV free days	3 (0 – 4)	2 (2 – 3)	U = 1287.5	0.026
ICU stay (d)	13 (8 – 16)	10 (7.25 – 11)	U = 603.5	0.004
Hospital stay (d)	18 (10 – 21)	13 (10 – 14)	U = 595.5	0.003
Morality at 30 days	16 (35.6%)	6 (14.3%)	X2 = 5.20	0.023
Morality at 90 days	18 (40.0%)	7 (16.7%)	X2 = 5.77	0.016

Data are presented as mean ± SD, median (IQR) or number (%). IQR: Interquartile range, T: Student's t test, U: Mann Whitney test

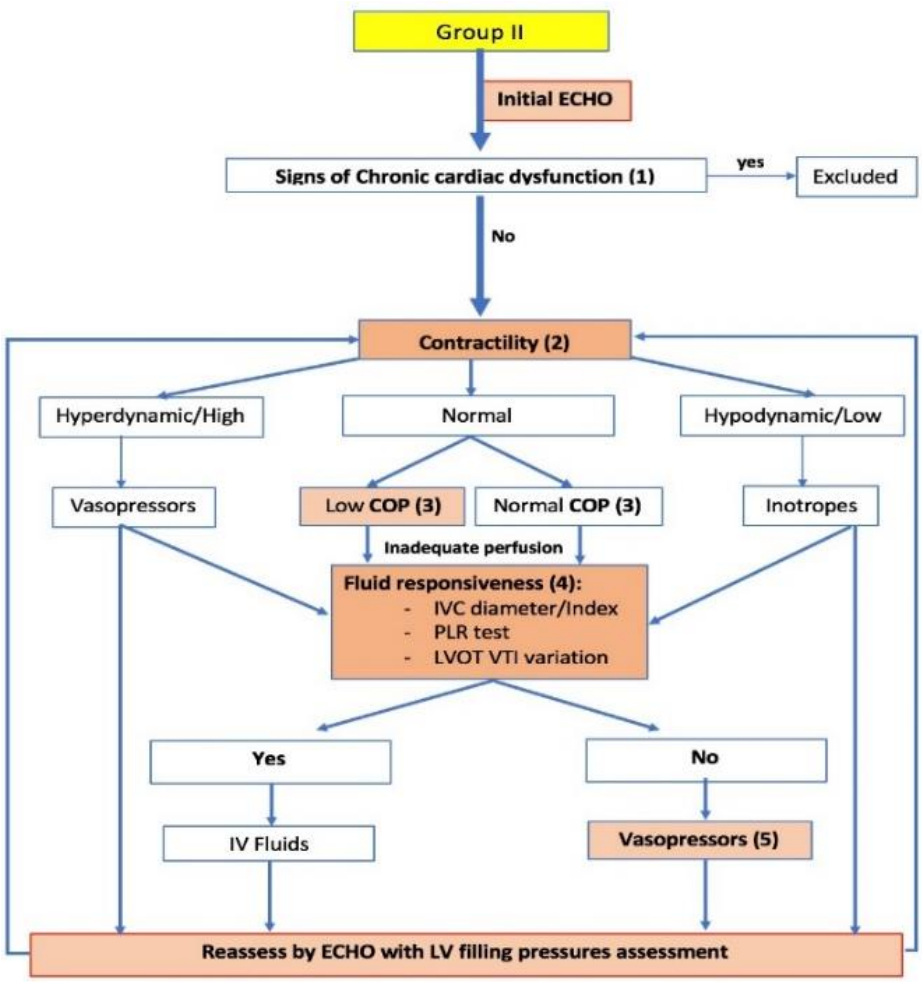

Figure 3: Echocardiography-guided algorithm in severe sepsis/septic shock.

CI: 1.137 - 2.404) at 30 and 90 days respectively in EGDT group compared to ECHO group.

4. Discussion

In the present work, we proposed that the use of ECHO to guide treatment of sepsis and septic shock will be associated with better outcome. Thus, we designed the present study to examine this hypothesis in the light of available gold standard of sepsis treatment (i.e. EGDT) at the time of the study. We prospectively evaluated a group of patients whose treatment was guided by ECHO and compared the results with a group of patients who received EGDT.

Our results regarding the mortality is comparable to those reported by Chertoff et al. [21] who reported a mortality rate of 29.69%. In addition, the reported

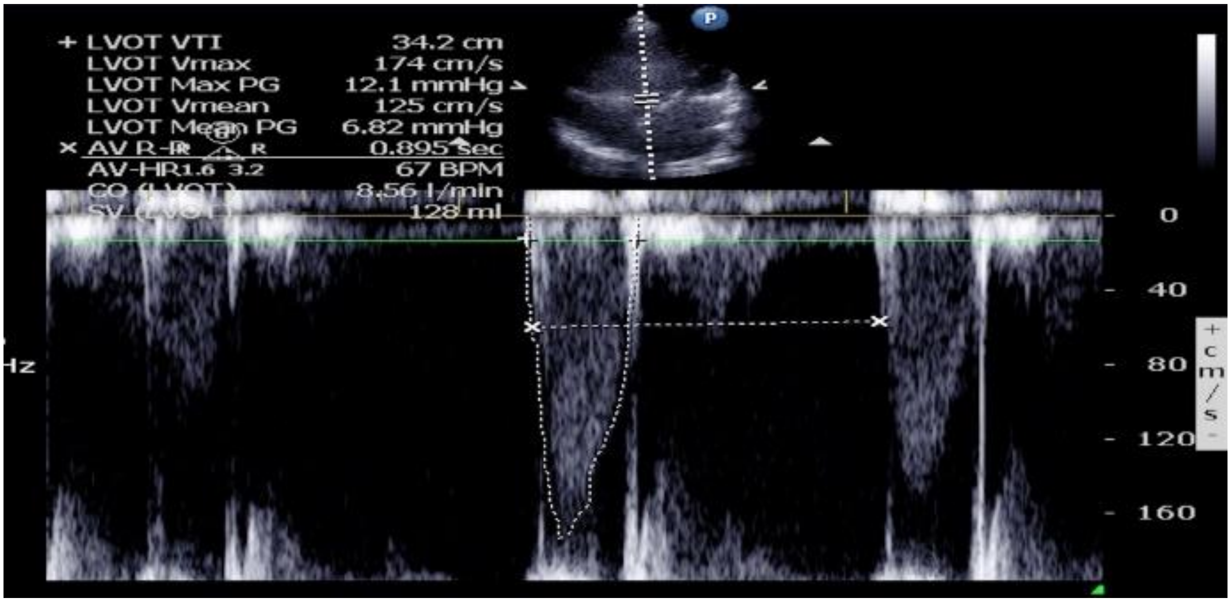

Figure 4: Cardiac output calculation using the left ventricular outflow tract (LVOT) velocity time integral (VTI) and LVOT cross sectional area (CSA)

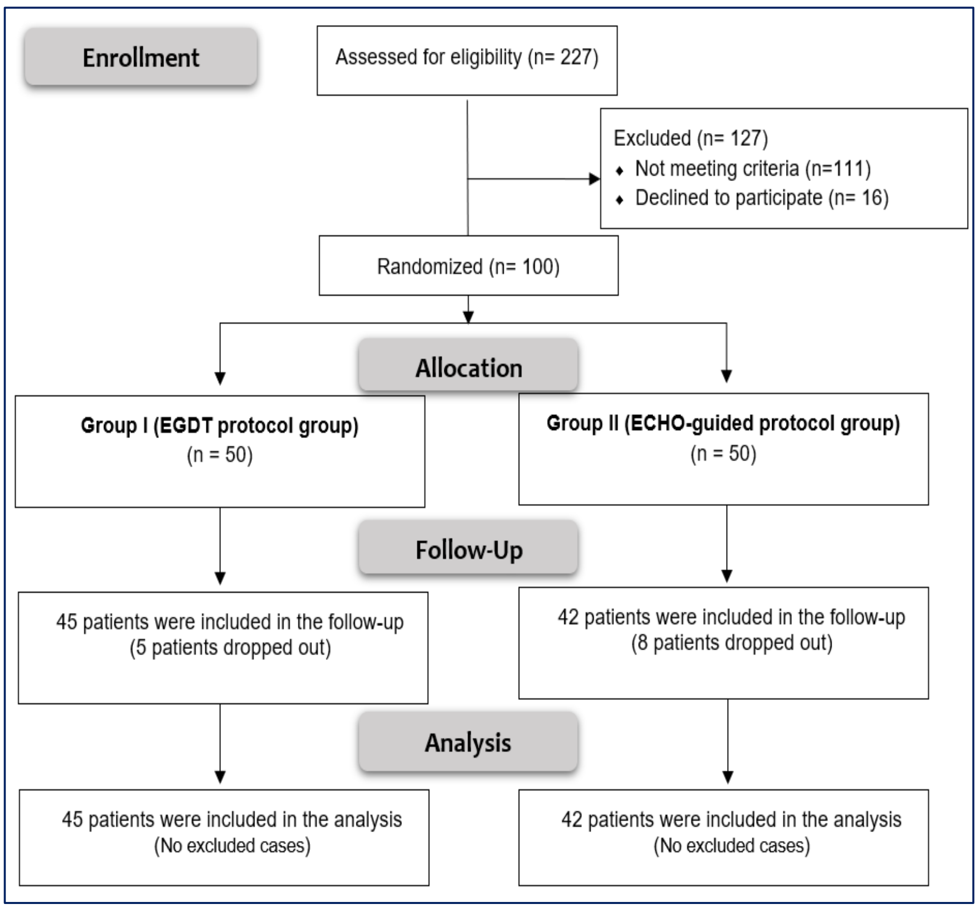

Figure 5: CONSORT flowchart of the study groups

incidence of mortality in the present work lies within reported range in literature; the short-term mortality is 20% to 30%, and up to 50% in patients with septic shock. [1, 22]

In contrary to Lanspa et al.[8] who reported insignificant difference between ECHO-guided resuscitation compared to EGDT in mortality, ICU stay or lactate clearance. This could be a result of late ECHO assessment after initial resuscitation as no difference in fluids administration between the two groups in contrary to our study results which showed a statistically significant difference between groups in the fluid resuscitation volume.

The present work revealed that the baseline MAP of both groups shows no significant difference. Then the MAP of the ECHO group became higher significantly than that of the EGDT group after 6 and 12 hours of the study. Thereafter, the MAP of both groups shows no significant difference at 24 hours from enrolment. This means that the ECHO group reached the target MAP earlier.

Lin and his colleagues observed improvement of blood pressure of the intervention group when they tested the effect of modified goal-directed protocol (targeting specific MAP, CVP and UOP without targeting ScvO2 on the clinical outcome of septic shock patients. However, the MAP of the intervention group stayed significantly higher throughout the study.[23]

In the current work, there was no statistically significant difference between both groups as regards the HR at the start of the study, then the HR starting from 6 hours till 24 hours after the enrolment differed significantly between both groups.

The significant decrease in the HR in the ECHO group was shown as well when the HR measurement was compared to the baseline HR at enrolment in the study. This decrease in the HR in the ECHO group can be a preceding indicator of the improvement of the hemodynamics which also correlated with higher MAP in the ECHO group.

The fluid therapy in the EGDT group was according to the CVP (targeting CVP between 8 - 12 mm Hg). This CVP guidance made the fluid therapy relatively higher in the EGDT group. Most of recent studies that test the CVP in guiding fluid therapy criticize the CVP as a predictor of fluid responsiveness as it may be falsely high in volume-depleted patient hindering useful fluid resuscitation or it may be falsely low in volume overloaded patient exposing the patient to more overload or even pulmonary congestion and edema. However, it is still used by many clinicians in ICU.

In agreement with our results, a study by Feng et al. [24] who reported that those who had transthoracic ECHO (TTE) had a higher maximum dose of norepinephrine, but surprisingly were weaned of vasopressors earlier compared to the no TTE group. Dobutamine was used more often in the group who received TTE, they concluded that performance of TTE is associated with a 28-day mortality benefit in a general population of septic, critically ill patients. [24] This is also in agreement with Kanji et al.[25] reported more utilization of dobutamine in the limited ECHO group compared to the standard management.

In the present study, we reported significantly lower total MV days, MV free days and ICU and hospital stays in ECHO group compared to EGDT group due to earlier weaning from vasopressors and MV.

This is in disagreement with Lanspa et al.[26] who reported an insignificant difference between the echo group and non-echo group (median of 28 days versus 25 days; p=0.51). Also, Feng et al. reported no significant difference in ventilation-free days between ECHO group and non-ECHO groups. [24]

Overall, results of the present work indicated that, ECHO as a sole monitoring and guiding tool was associated with better outcome than EGDT as evidenced from enhancement of vital data over time, decreased total fluid administration, significant decrease of 30 day and overall mortality. Critical care echocardiography may be considered the fifth pillar of clinical examination especially in critically ill patients.[27,28]

Finally, it may be the first time to compare outcome between EGDT and use of echocardiographic findings to govern the progress of management in sepsis and septic shock. Results of the present work seems to be promising. However, further studies with larger sample size and in multi-centers are needed to generalize the routine use of echocardiography in management of hemodynamics in severe sepsis and septic shock provides. Anyway, present work advocates routine uses of echocardiography as a crucial, non-invasive bedside tool for the management of patients with severe sepsis and septic shock.

Another limitation of our study is the use of old definitions of sepsis, sever sepsis and septic shock and it's preferred to depend on the new definitions for sepsis and septic shock provided by the International Consensus (Sepsis-3) in 2016. [29]

Further studies are needed to reveal the role of early diagnosis by new scores as Quick Sequential Organ Function Assessment (qSOFA) and qSOFA-65, which helps in prediction and thereby early management.[30]

5. Limitations

Limitations in the routine use of ECHO still exist. There is low echogenicity at surface examination. For continuous monitoring of cardiac output or pulmonary artery pressure, ECHO is not the right tool. Also, in centers where adequate training on the use of critical care ECHO does not exist, and when repeated bedside assessments of hemodynamic variables are required it is of limited use as a single monitoring tool. Patients excluded from the study e.g. morbid obese and atrial fibrillation still represent challenges in echocardiographic assessments and follow up either due to inconsistency of cardiac output on LVOT VTI or limited window for examination respectively.

6. Conclusion

In severe sepsis and septic shock, ECHO-guided management of hemodynamic provides additional benefits over early goal-directed therapy. It is a non-invasive, reproducible, readily available tool with a resultant decrease in mortality and favorable outcomes in the term of lower total fluid intake, earlier weaning off vasopressors and less mechanical ventilation days, ICU and hospital stay. ECHO-guided management should be a routine care in the management of hemodynamics in severe sepsis and septic shock patients as early as possible in the first 24 h.

Conflicts of Interest

There was no conflict of interest. No external funding was used for this study.

Author Contributions

WSA: Study design, manuscript writing, data collection

OMS: Manuscript writing, data collection

ASE: Study design, Manuscript editing, review, data collection

MSA: Manuscript editing, review, data collection

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