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Limited echocardiography–guided therapy in subacute shock is associated with change in management and improved outcomes ☆,☆☆

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ABSTRACT

Purpose: The purpose of the study was to compare the effect of limited echocardiography (LE)–guided therapy to standard management on 28-day mortality, intravenous fluid prescription, and inotropic dosing following early resuscitation for shock.
Materials and methods: Two hundred twenty critically ill patients with undifferentiated shock from a quaternary intensive care unit were included in the study. The LE group consisted of 110 consecutive patients prospectively studied over a 12-month period receiving LE-guided management. The standard management group consisted of 110 consecutive patients retrospectively studied with shock immediately prior to the LE intervention.
Results: In the LE group, fluid restriction was recommended in 71 (65%) patients and initiation of dobutamine in 27 (25%). Fluid prescription during the first 24 hours was significantly lower in LE patients (49 [33-74] vs 66 [42-100] mL/kg, $P = .01$), whereas 55% more LE patients received dobutamine (22% vs 12%, $P = .01$). The LE patients had improved 28-day survival (66% vs 56%, $P = .04$), a reduction in stage 3 acute kidney injury (20% vs 39%), and more days alive and free of renal support (28 [9.7-28] vs 25 [5-28], $P = .04$).
Conclusions: Limited echocardiography–guided management following early resuscitation is associated with improved survival, less fluid, and increased inotropic prescription. A prospective randomized control trial is required to verify these results.

1. Introduction

Despite a significant mortality rate, there exists no standard management algorithm for patients following initial resuscitation for shock. The underlying etiology of undifferentiated shock remains predominantly sepsis; and therefore, the Surviving Sepsis efforts (www.survivingsepsis.org) are primarily used to guide initial care [1]. The focus of this study is the period after the treating team has achieved the targets recommended in these guidelines, when intravenous fluid administration has resulted in a central venous pressure (CVP) of 8 to 12 mm Hg and the patient requires ongoing vasopressor support to achieve a mean arterial pressure of at least 65 mm Hg.

Although intravenous fluid is essential to restore perfusion in shock, once the circulation has been adequately expanded, additional fluid results in tissue edema, longer mechanical ventilation (MV), acute kidney injury (AKI), and an increased risk of death [2–4]. Currently, there is no uniform diagnostic approach able to reliably determine which patients will or will not increase organ perfusion in response to additional fluids [5]. In addition to intravenous fluids, inotropes are sometimes added as adjunctive therapy when left ventricular systolic dysfunction is believed to be the cause of inadequate organ perfusion. A 25% incidence of inotrope-induced arrhythmia mandates the use of inotrope only when necessary [1].

Limited echocardiography (LE) is defined in this study as standard parasternal long- and short-axis, apical 4-chamber, and subcostal views with color-flow Doppler and without alternate views. Easily accomplished within 5 to 10 minutes at the bedside, LE provides the treating team with a real-time recommendation for fluid management and the need to add an inotrope [6,7]. Despite the widespread integration of limited echocardiography into clinical practice, there are very limited data on clinical outcomes [8]. We hypothesized that LE-based recommendations for intravenous fluid and inotropes would improve survival compared to standard management in patients with undifferentiated vasopressor-dependent shock. We also hypothesized

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mechanisms through which LE improved outcomes may include reduction in the incidence of AKI and reduced days spent on MV.

2. Materials and methods

2.1. Patients

This study was performed at a quaternary-level hospital (St Paul's Hospital in Vancouver, British Columbia) intensive care unit (ICU) that is the regional cardiovascular center. The study included 220 patients referred to the critical care service with vasopressor-dependent shock despite an intravenous fluid challenge achieving a CVP of at least 8 mm Hg. The intervention arm of the study was conducted over a 12-month period (January 4 to Dec 31, 2012). One hundred ten patients in the intervention arm had an LE performed using a handheld device (V-Scan; GE Healthcare, Pittsburgh, PA), and 110 patients were managed in standard fashion (defined below). All patients were initially mechanically ventilated. Limited echocardiography was performed within 24 hours of admission to the ICU and within 36 hours of admission to the hospital. Study results and recommendations from the LE were communicated verbally and in written format to the treating team during the morning intake rounds. This study was approved by the Providence Health care research ethics board, and consent was waived.

2.2. Protocol

Echocardiography was performed by 1 of 3 intensivists with advanced training (American College of Cardiology Level II) in echocardiography. In no instances were they also the attending physician for the patient. Limited echocardiography included the parasternal long axis to assess aortic and mitral valve function, parasternal short axis at the level of the papillary muscle insertion to assess global left ventricular systolic function, the 4-chamber apical view for left and right ventricular size and function, and the subcostal view to assess the inferior vena cava (IVC) size and respiratory variability and for pericardial fluid. In cases with poor parasternal or apical windows, the equivalent views were obtained from the subcostal approach. In our institution, the outpatient echocardiography laboratory uses "eye-ball" approximation of ventricular function rather than a calculated value via the Simpson method given the excellent correlation in these values. We chose to adopt this well-validated approach [9,10].

Left and right ventricular systolic function was graded as normal, moderate (left ventricular ejection fraction [LVEF] 30%-45%), or severe systolic dysfunction (LVEF <30%). The pericardium was assessed for evidence of effusion or possible tamponade, whereas the IVC diameter's fluctuation with respiration was graded as either less than or greater than 15%. Treatment recommendations were 1 of 4 depending upon the LE: (1) less than 15% fluctuation of the IVC diameter (dIVC) with respiration and normal left ventricular function = discontinue fluid administration and continue vasopressors alone; (2) greater than 15% dIVC and normal left ventricular function = 20 to 40 mL/kg intravenous fluid administration; (3) greater than 15% dIVC and moderate to severe left ventricular dysfunction = 10 to 20 mL/kg intravenous fluid and dobutamine 5 μg/(kg min); (4) moderate to severe left ventricular systolic dysfunction and a dIVC less than 15% = dobutamine 5μg/(kg min) and fluid restriction. Right ventricular dysfunction was deemed present if there was bowing of the intraventricular septum throughout the cardiac cycle and a right ventricle at least as large as the left ventricle in the apical 4-chamber view. Valvular pathology was noted and graded as per American Society of Echocardiography guidelines only using color Doppler and observation of valve motion. If compatible with severe valvular stenosis or regurgitation, a formal echocardiogram was requisitioned and performed for a compete assessment.

One hundred ten consecutive patients admitted prior to January 4, 2012, with non–LE-guided, standard management of shock were enrolled into this study following informed consent to review records from the critical care research database. St Paul's Hospital standard shock guidelines adhere closely to the 2012 Surviving Sepsis guidelines [11]. They suggest 20 to 40 mL/kg initial intravenous fluid and further fluids as appropriate. A central line is placed in the jugular or subclavian positions, and intravenous fluid is administered until a CVP of 8 to 12 mm Hg is achieved. Further fluid boluses are at the discretion of the treating team. Noradrenaline is the suggested initial vasopressor if the mean arterial pressure remains below 65 mm Hg. Once patients are transferred to the ICU, dobutamine may be added for a central venous oxygen saturation less than 70% and evidence of ongoing hypoperfusion (urine output < 0.5mL/[kg h] or an arterial lactate > 2 mmol/L). This control population was chosen to avoid bias from the intervention (in a nonrandomized or blinded trial) and to acquire the most representative population in which to assess the intervention.

2.3. Statistical analysis

The primary outcome was 28-day mortality. Secondary outcomes included fluid prescription during the first 4 days and measurement of organ dysfunction, calculated as days alive and free of renal replacement therapy (RRT) or MV [12]. Patients with end-stage renal failure were excluded from the days alive and free of RRT. All patients were classified according to the current Kidney Disease: Improving Global Outcomes guidelines for AKI based on serum creatinine (SCr) (www.kdigo.org). An *AKI (stage 1)* was defined by SCr rise of at least 26.5 μmol/L within 48 hours or SCr increase of at least 1.5-fold from the baseline reference value. *Stage 2 AKI* was defined as a 2.0- to 2.9-fold increase from baseline reference SCr. *Stage 3 AKI* was defined as an at least 3-fold increase from baseline reference SCr, or an increase of 354 μmol/L, or commenced on RRT irrespective of stage of AKI. The reference SCr is defined as the lowest creatinine value recorded within 3 months of the event, or from repeat SCr within 24 hours, or estimated from the nadir SCr value if a patient recovers from AK. Patients with chronic kidney disease at admission were excluded.

Our primary analysis used Kaplan-Meier estimation of survival function; univariate analyses was performed using χ^2 for categorical data and either Kruskal-Wallis tests or *t* tests for continuous data. All tests were 2-sided. Differences in baseline characteristics were considered significant if $P < .05$ and were subsequently used in a Cox proportional hazards model to determine the risk of mortality associated with LE. Although nonsignificant, we forced the Acute Physiology and Chronic Health Evaluation (APACHE) II score as a covariate in the statistical model. Subgroups according to etiology of shock were analyzed using stratified Cox regression and the Breslow method of ties. All analyses were performed using R (version 2.8.1, www.R-project.org) and SPSS version 16.0 (SPSS Inc., Chicago, IL) statistical software packages.

3. Results

A total of 220 patients were included in this study: 110 in the LE cohort and 110 in the standard management group. All patients were followed up to 28 days for mortality, with outcome data available for all patients included in the study. Table 1 describes the baseline LE patients compared to standard management. As markers of chronic health, APACHE II, age, and the presence of chronic organ failures influence outcome independently of intervention. The LE and standard management groups did not differ with respect to these variables. The discharge diagnosis pertaining to the cause of shock was predominantly vasodilatory (78% LE and 75% standard management) followed by cardiac (12% LE and 15% standard management).

Table 1
Patient demographics

Demographics	LE (n = 110)	Standard (n = 110)	*P*
Age (y)	63 (50-73)	66 (55-75)	.27
Gender, n (%) female	44 (40)	32 (30)	.10
APACHE II	23 (19-29)	24 (18-29)	.73
BMI	28.6 (24-34)	28.2 (25-33)	.97
Cause of shock, n (%)			
Vasodilatory	86 (78)	83 (75)	.38
Cardiac	14 (12)	16 (15)	.21
Hemorrhage	3 (3)	5 (5)	.45
Mixed	7 (6)	7 (6)	.14
Preexisiting conditions, n(%)			
CHF (LVEF < 35%)	6 (5)	5 (4)	.95
Chronic renal disease	11 (15)	17 (17)	.68
Physiology (ICU admission)			
Fluid ml/kg prior to ICU	68 (58-76)	65 (55-72)	.90
AKI stage 3, n (%)	10 (9)	12 (11)	.73
Mean arterial pressure	62 (55-70)	67 (60-73)	.003
CVP (mm Hg)	13 (9.0-15)	13 (10-16)	.47
Heart rate	110 (92-125)	110 (96-125)	.48
Norepinepherine (μg/min)	10 (5.0-16)	12 (6.0-24)	.06
Laboratory variables			
White blood cell count (10^3/mm^3)	12 (9.0-20)	11 (7.0-16)	.23
Platelet count	176 (120-250)	176 (94-250)	.26
Pao_2/Fio_2 ratio	181 (130-280)	219 (160-270)	.15
Creatinine	141 (80-240)	112 (74-250)	.18
Bilirubin	13 (7.0-28)	13 (7.0-28)	.92
Lactate	1.6 (1.1-3.0)	1.4 (1.1-3.0)	.90
pH	7.27 (7.20-7.30)	7.29 (7.20-7.30)	.35
Na+	137 (130-140)	140 (140-140)	.39
Urea	10.7 (7.3-20)	10.9 (6.8-18)	.76
Hematocrit	0.29 (0.25-0.33)	0.29 (0.26-0.66)	.36

Values are reported as median (interquartile range); significance = $P < .05$. BMI indicates body mass index; CHF, congestive heart failure.

The remaining cases were mixed cardiac/vasodilatory or initially occult bleeding. No significant differences were noted between groups with respect to cause of shock. In the LE group, during the first day of admission, the lowest mean arterial pressure was slightly lower than standard management (62 [55-70] mm Hg vs 67 [60-73] mm Hg in those with standard management). Laboratory values associated with severity of presentation including arterial pH and lactate were not different between groups (Table 1).

3.1. LE findings

In the LE group, 19% of patients had findings compatible with significant valvular abnormalities (Table 2). None of these required cardiothoracic procedures to reverse the disease. Twenty-five percent of patients had severely depressed LVEF. Diameter of IVC was less than 15% with respiration in 65% of cases, suggesting an extremely low probability of augmenting forward flow with additional fluids. Moderate to severe right ventricular dysfunction was observed in 9% of cases.

Table 2
LE findings and management suggestions

Findings	LE (n =110)
Time (h) to LE from ED admission med (IQR)	11 (7.5-15)
Significant valvular pathology, n (%)	14 (19)
Moderate-severe LV failure, n (%)	27 (25)
IVC collapsability	
<15%, n (%)	71 (65)
>15%, n (%)	39 (35)
Significant pericardial effusion, n (%)	0 (0)
RV dysfunction (moderate to severe), n (%)	34 (30)
Suggested change in management	
Restrict fluid, n (%)	71 (65)
Add inotropes, n (%)	27 (25)

IQR indicates interquartile range; LV, left ventricle; RV, right ventricle.

3.2. LE-based treatment

The most common recommendation (Table 2) was to restrict fluid administration (65%) followed by the addition of inotropic therapy (25%). In this cohort, 6 (5%) patients had repeat studies at the request of the treating team. All of these studies were more than 7 days following the initial LE.

3.3. Fluid and inotrope prescription

Reflecting the 65% recommendation to discontinue fluid administration in the LE group, fluid administration was significantly lower ($P = .04$) during the first 24 hours of therapy following completion of early goal-directed therapy (LE vs standard management, 49 [33-74] vs 66 [42-100] mL/kg). Fluid administration was not significantly different between groups during days 2 to 4 (Table 3) . Urine output in the LE group was greater in each of the 4 days following admission (Fig. 1), but this did not reach statistical significance. Despite an equal incidence of known congestive heart failure (Table 1), 22% of patients received dobutamine in the LE group compared to 12% with standard management ($P = .01$).

3.4. Clinical outcomes

Kaplan-Meier 28-day survival analysis favored patients receiving LE, with a 28-day survival rate of 66% vs 56% ($P = .04$) in the standard management group (Fig. 2). Using Cox regression analysis to control for the unmatched variables in Table 1 (mean arterial pressure) as well as severity of illness upon presentation (APACHE II), we found that performing LE was associated with a lower risk of death with a hazard ratio (HR) of 0.64 (0.41-0.98) ($P = .014$). Patients treated with LE also had more days alive and free of renal support (28 [9.7-28] vs 25 [5-28], $P = .04$) compared to standard management. Limited echocardiography was also associated with a reduction in the incidence of any AKI (68%) vs standard management (95%) and with more grade 3 AKI (20% LE vs 39% standard management) (Table 4). The LE cohort did have a nonsignificant trend towards more days alive and free of MV (20 [3-27] vs 18 [2.0-26], $P = .565$). As expected, an increase in APACHE II (HR 1.07 [1.04-1.10], $P = .02$) was associated with an increased hazard for mortality (Table 5). We performed Cox regression stratified by the cause of shock and found that the protective effect was similar for all causes, with cardiac and hemorrhagic causes reaching statistical significance (Table 5).

3.5. LE-derived dIVC vs CVP or volume infused prior to ICU admission

We compared the usual clinical measures of volume status (CVP and volume of fluid previously administered in the emergency department [ED]) to a dIVC ultrasound-based approach. As shown in Fig. 3, the receiver operating characteristic for CVP compared to dIVC is 0.42, whereas that of the volume of fluid administered in the

Table 3
Intravenous fluid and dobutamine prescription during days 1 to 4

Therapy	LE (n = 110)	Standard (n = 110)	*P*
Intravenous fluid day 1 (mL/kg)	49 (33-74)	66 (42-100)	.04
Intravenous fluid day 2 (mL/kg)	47 (32-66)	44 (29-59)	NS
Intravenous fluid day 3 (mL/kg)	42 (29-51)	34 (25-45)	NS
Intravenous fluid day 4 (mL/kg)	36 (26-49)	40 (27-49)	NS
Dobutamine, n (%)	24 (22)	14 (12)	.01

NS indicates not significant.

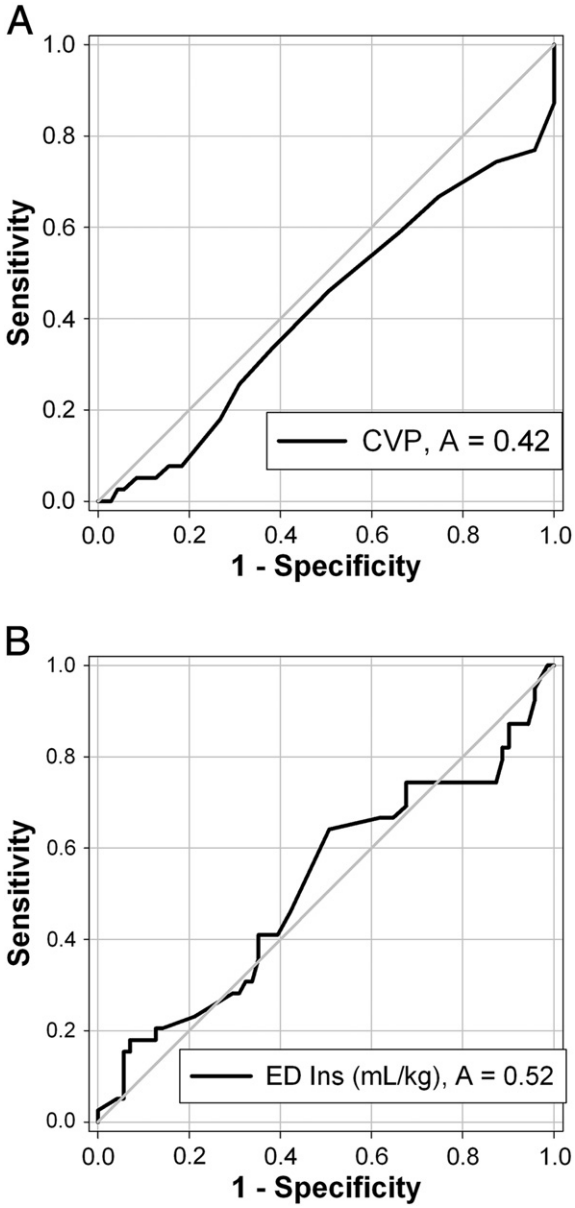

Fig. 1. Central venous pressure and fluid administered in the ED vs dIVC. A and B, Receiver operating curves compare CVP and ED fluid administration to a dIVC of greater than 15%, assuming the dIVC is the true estimate of fluid responsiveness (A). The area under the CVP curve is 0.42, whereas that of the ED fluid intake is 0.52 (B).

ED is 0.52, suggesting that neither CVP nor volume of fluid administered can serve as surrogates for dIVC. Overall, there is no correlation between CVP and dIVC. Thus, the usual clinical measures of volume status are generally poor predictors for LE-derived dIVC or (lack of) volume responsiveness.

4. Discussion

The major finding in this study is that the use of LE to guide subsequent fluid and inotropic therapy in patients, whose shock has been initially resuscitated with fluids and noradrenaline, is associated with decreased mortality compared to standard management. Limited echocardiography was also associated with a decrease in initial fluid prescription and an increase in dobutamine use. The most pronounced therapeutic effect of LE-guided treatment was a reduction in stage 3 AKI and an increase in days alive and free of RRT.

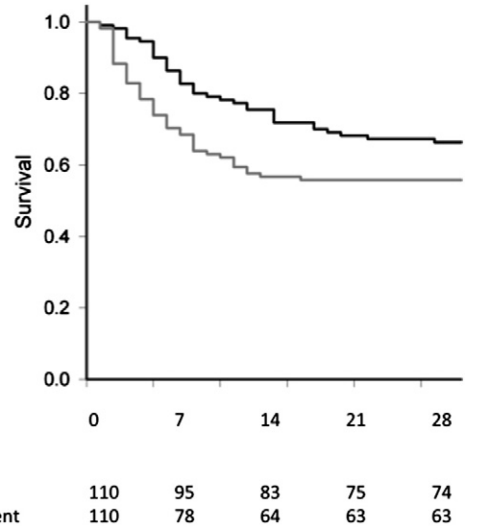

Fig. 2. Black line = LE-guided therapy; gray line = standard management. Kaplan-Meier estimates of mortality over 28 days. The rate of mortality was significantly higher in the standard treatment group ($P = .04$).

Early aggressive resuscitation of mixed shock with intravenous volume expansion, vasopressors, and inotropes became widely adopted following the landmark study of Rivers et al [2] in 2001. Although securing central venous access and aggressive fluid administration have become standard of care over the first 6 to 12 hours [13], the subacute phase of resuscitation is more elusive. Administration of intravenous fluids in quantities sufficient to achieve a CVP of 8 to 12 mm Hg (13 mm Hg in the original study [2]) is integral to early goal-directed therapy. However, after this has been achieved, CVP is unable to predict an increase in cardiac output or organ perfusion in response to further fluid [5]. Furthermore, in our study, we illustrate the poor correlation between traditional means of volume status, namely, CVP, and markers of volume responsiveness such as dIVC. Without a standardized method allowing the clinician to determine whether further fluid prescription will augment perfusion, there may be a tendency to err on the side of additional bolus fluids while the patient remains on vasopressors, possibly causing more harm than benefit [4]. How to introduce and titrate inotropes is equally problematic. The guideline recommends the use of central venous oxygen saturation, but it is a poor predictor of cardiac performance in noncardiogenic causes of shock [14]. Inotropic therapy is not without significant adverse effects, as up to 25% of patients experience serious tachyarrythmias [1]. The treating team is therefore faced with 2 questions for their patients with continued vasopressor-dependent shock. First, will further fluids improve perfusion; and second, does the patient require additional inotropic support? Bedside echocardiography is unique in that it can answer both of these questions immediately and noninvasively.

Table 4
Survival and days alive and free of life support

Outcomes	LE (n = 110)	Standard (n = 110)	*P*
28-d survival, n (%)	73 (66)	62 (56)	.04
Days alive and free from MV	20 (3.0-26)	17 (2.0-26)	.57
Days alive and free of RRT	28 (10-28)	26 (5.0-28)	.07
AKI	**LE (n = 95)**	**Standard (n = 93)**	
Any AKI, n (%)	65 (68)	88 (95)	.001
AKI stage 1, n (%)	32 (34)	34 (37)	.34
AKI stage 2, n (%)	14 (15)	18 (19)	.57
AKI stage 3, n (%)	19 (20)	36 (39)	.013

MV = mechanical ventilation, RRT = renal replacement therapy, AKI = acute kidney injury.

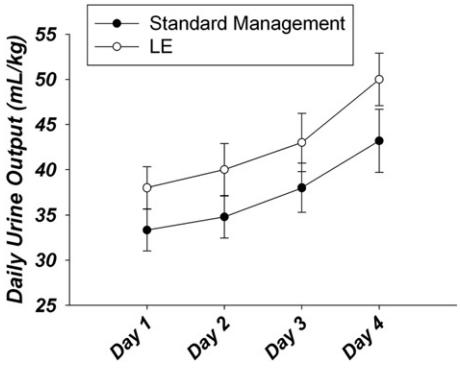

Fig. 3. Daily urine output. Urine output (in milliliters per kilogram) is plotted in the 2 groups over the first 4 days following admission. Although a clear trend emerges of increased urine output in the LE group, the effect is not significant ($P > .05$) at any time point.

Bedside echocardiography in critically ill patients has been in practice for well over 2 decades [15]. With dramatically improved technology and integration in training fellowship programs, physician-led acute bedside or point-of-care echocardiography is now becoming commonplace [16]. Noncardiologists can be trained to perform bedside echocardiography with good accuracy in critically ill patients [17]. In fact, very basic critical care echocardiography can be taught to medical residents with good reliability in less than 12 hours [18]. Both transthoracic and transesophageal echocardiography can be used in critically ill patients, and using either method has been shown to alter management of critically ill patients in a significant number of cases [19,20]. However, whether echocardiography-guided changes in management modify outcome is not certain. Surprisingly, there is very little literature that relates echocardiography to clinical outcomes. There are numerous protocols for bedside echocardiography in critically ill patients, ranging from a complete study suitable for outpatient echocardiography to very abbreviated forms [9,10,21]. Our clinical service decided upon a pragmatic approach to allow 10 minutes to determine right and left ventricular systolic function, assess volume status using the respiratory variability of IVC diameter, and screen for pericardial and major valvular disease. Two major studies examined the correlation between the increase in IVC diameter (ΔD_{IVC} is the fractional increase in IVC diameter) with positive pressure ventilation and the likelihood of an increase in cardiac output in response to further intravenous fluids. Barbier et al [22] reported that a ΔD_{IVC} of > 18% best defined those who experienced an increased cardiac output with volume expansion, whereas Feissel et al [23] found a ΔD_{IVC} of greater than 12% was able to predict volume responsiveness in their mechanically ventilated patients. The clinical service defined a *high likelihood of volume responsiveness* as a ΔD_{IVC} of greater than or equal to 15%.

Table 5
Cox proportional hazards analysis of variables influencing mortality

	HR	95% CI
Variable		
LE	0.64*	0.41-0.98
Age	1.01*	1.0-1.02
APACHE II	1.07*	1.04-1.10
Subgroup (stratified analysis)		
Vasodilatory	0.60	0.35-1.03
Cardiac	0.58*	0.34-0.99
Hemorrhagic	0.59*	0.34-0.99
Mixed (vasodilatory and cardiac)	0.61	0.36-1.04

* $P < .05$.

Limited echocardiography in this study found moderate to severe left ventricular dysfunction in 25% of patients. This may be in fact lower than previously reported estimates of the incidence of severe left ventricular hypokinesia in septic shock [24]. The direct estimation of LVEF by LE was associated with a 55% increase in the use of dobutamine compared to those treated with standard management. Although the use of dobutamine titrated to oxygen consumption has not been of benefit to patients in subacute shock, there has yet to be a randomized controlled trial using ultrasound quantification of LVEF to initiate dobutamine in vasopressor-dependent shock [25]. It is interesting to note that, in a systematic review of patients at high risk of AKI, the most protective intervention was the addition of an inotrope [26]. We feel our improved results compared to previous studies examining the addition of inotropes in shock may be attributable to the improved diagnostic accuracy with ultrasound vs indirect and time-delayed measures of cardiac performance such as oxygen consumption.

Limited echocardiography evaluations of our patients resulted in a recommendation of fluid restriction in the majority of our patients. This fluid restriction is similar to the findings of a recent small study in which superior vena caval respiratory fluctuation using transesophageal echocardiography was compared to CVP-based guidelines [27]. In this study, LE led to a 33% reduction in fluid administration during what may be considered the critical first day of ICU admission. Other investigators have found that conservative fluid strategies favor survival and decrease time spent on MV in patients with acute respiratory distress syndrome as well as those with acute lung injury [3,28]. It is also proposed that high venous pressures created through excessive fluid administration worsen renal function acutely and may prevent subsequent recovery [26,29,30]. Furthermore, in patients with septic shock, it appears that less volume expansion may be associated with a survival advantage [4,31]. Taken together with our data, we feel that it is probable that the fluid limitation as a result of LE, together with matching inotropic support to those most in need, may be in part responsible for improvement in both survival and renal function.

This study has several limitations. The major limitation is its nonrandomized nature. The use of historical controls poses the unavoidable risk of unappreciated confounders, in particular a systematic change in management being responsible for differences in outcome. We strove to identify and compare the major clinical confounders that are known to influence organ failure and mortality in shock. Presenting severity of illness, age, and comorbid conditions appeared well matched between groups and controls. In addition, we chose a priori to include all consecutive patients immediately prior to the intervention to include the most comparable population. With respect to the ongoing validity of information provided by a single LE study throughout the patient's stay, this study was not designed to answer this question, which would require repeated studies throughout the period of shock. Lastly, our practice locally is to use fluids and noradrenaline for early goal-directed therapy in the ED; so no dobutamine is initiated until the patient arrives in the ICU or admitted to the service. Although this provided us an opportunity to determine the prescription of dobutamine through LE performed in (or by) the ICU, our approach may not be applicable to centers that begin dobutamine earlier in the resuscitation.

We conclude that LE-guided resuscitation following early resuscitation for shock is associated with improved 28-day survival. The most important information derived from the LE was a combination of LVEF and Inferior Vena Cava Collapsibility Index (IVC-CI) that significantly influenced volume and inotropic prescription in this population. Given no significant effect upon duration of MV and a large (19%) reduction in stage 3 AKI with LE, it is probable that avoidance of advanced renal failure is one mechanism through which LE improves survival. A prospective randomized control trial is required to verify these results.

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