Resuscitation of the Critically Ill in the ED: Responses of Blood Pressure, Heart Rate, Shock Index, Central Venous Oxygen Saturation, and Lactate

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To describe the simultaneous responses of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), heart rate (HR), shock index (SI = HR/SBP), central venous oxyhemoglobin saturation ($ScvO_2$), and arterial blood lactate concentration (Lact) to resuscitation of critically ill patients in the emergency department (ED), an observational descriptive study was conducted in the ED of an urban teaching hospital. Thirty-six patients admitted from the ED to the medical intensive care unit were studied. Vital signs were measured immediately on arrival to the ED (phase 1). After initial resuscitation and stabilization, ie, HR between 50 and 120 beats/min and MAP between 70 and 110 mm Hg (phase 2), $ScvO_2$ and Lact were measured and additional therapy was given in the ED to increase $ScvO_2$ to >65% and decrease Lact to <2 mmol/L, if needed (phase 3). SBP, DBP, MAP, HR, SI, $ScvO_2$, and Lact were measured. Initial resuscitation increased SBP from 103 ± 39 to 118 ± 29 mm Hg ($P < .05$) but did not affect DBP (53 ± 35 to 63 ± 22 mm Hg, P = NS), HR (110 ± 26 to 110 ± 22 beats/min, P = NS) or SI (from 1.3 ± 0.7 to 1.0 ± 0.3, P = NS) from phase 1 to phase 2. $ScvO_2$ remained <65% and/or Lact >2.0 mmol/L in 31 of 36 patients at phase 2, and additional therapy was required. Lact was decreased (from 4.6 ± 3.8 to 2.6 ± 2.5 mmol/L, $P < .05$) and $ScvO_2$ was increased (from 52 ± 18 to 65 ± 13%, $P < .05$) without significant additional changes in SBP, DBP, MAP, HR, or SI at phase 3. The in-hospital mortality was 14% for this group of patients. It was concluded that additional therapy is required in the majority of critically ill patients to restore adequate systemic oxygenation after initial resuscitation and hemodynamic stabilization in the ED. Additional therapy to increase $ScvO_2$ and decrease Lact may not produce substantial responses in SBP, DBP, MAP, HR, and SI. The measurement of $ScvO_2$ and Lact can be utilized to guide this phase of additional therapy in the ED. (Am J Emerg Med 1996;14:218-225. Copyright © 1996 by W.B. Saunders Company)

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Identification and therapy of critically ill patients in the emergency department (ED) is commonly guided by detection and correction of abnormal vital signs, although they correlate poorly with systemic perfusion and oxygenation.[1,2] A study has indicated that the majority of critically ill patients who were resuscitated to stabilize vital signs and normalize heart rate (HR) to between 50 and 120 beats/min, mean arterial pressure (MAP) to between 70 and 110 mm Hg, and central venous pressure (CVP) to between 15 and 30 mm Hg had reduced central venous oxyhemoglobin saturation measured in the right atrium ($ScvO_2$ <65%) and elevated arterial blood lactate concentration (Lact >2 mmol/L) in the ED. Systemic oxygen delivery and consumption are direct markers of the adequacy of systemic oxygenation in critically ill patients.[2] Acute decrease in systemic oxygen delivery and/or consumption are reflected by abnormal reduction of $ScvO_2$ and elevation of Lact, which are widely accepted as reliable, albeit *indirect,* markers of deficient systemic oxygenation.[3,4] Additional measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), temperature, and respiratory rate, as well as HR, on arrival to the ED were also found to be unreliable for identifying critically ill patients in need of immediate treatment and admission to the intensive care unit (ICU).[5] That particular study also hinted that the shock index (SI) (or the ratio of HR to SBP) of 0.9 or higher had a better sensitivity than individual measurements of HR or SBP to identify critically ill patients in the ED. However, the use of the SI alone to identify critically ill patients was disappointing because of its low sensitivity.

The present study examined simultaneous responses of SBP, DBP, MAP, HR, SI, $ScvO_2$, and Lact during resuscitation of critically ill patients in the ED. The hypothesis is that the additional therapy required to restore systemic oxygenation after initial hemodynamic stabilization is not easily determined by routine measurements of vital signs in the majority of critically ill patients treated in the ED.

METHODS

The study was approved by the Institutional Review Board for Human Research of Henry Ford Hospital. The

inclusion criteria were triage for an immediate treatment priority on arrival to the ED and admission to the medical ICU from the ED for continued therapy. Exclusion criteria were out-of-hospital cardiopulmonary arrest, age younger than 18 years, pregnancy, and patients presenting after trauma (penetrating or blunt) or with acute surgical emergencies. The latter category was excluded from the study because this group of patients frequently required rapid transportation from the ED for operative treatment or specialized diagnostic studies after initial resuscitation and hemodynamic stabilization. Thirty-six consecutive patients who met both criteria of critical illness were studied in the ED and the time course of the study was divided into three sequential phases according to predefined end points of therapy at each phase (Figure 1).

Arrival to ED and Triage (Phase 1)

Patients arrived at the ED by emergency medical services and none of the critically ill patients received any standard prehospital resuscitation other than supplemental oxygen and, in some cases, peripheral intravenous cannulation. Vital signs were measured immediately on arrival at the ED and before the initiation of in-hospital resuscitation. All patients in this study were allocated immediate treatment priority after triage.

Resuscitation and Stabilization of Vital Signs and Hemodynamics (Phase 2)

Initial resuscitation and hemodynamic stabilization followed a standard protocol (Table 1). Supplemental oxygen to maintain peripheral pulse oximetry greater than 97%, endotracheal intubation and mechanical ventilation (for airway protection, relief of respiratory distress, refractory hypoxia, or an increasing arterial P_{CO_2} >60 mmHg), fluids (0.9% normal saline and albumin), and packed red cell concentrate (guided by CVP and blood hemoglobin concentration) were used for resuscitation and hemodynamic stabilization. Morphine, sublingual nitroglycerin, intravenous furosemide, dopamine, dobutamine, and norepinephrine were also used if needed to stabilize MAP (from 70 to 110 mmHg), HR (from 50 to 120 mm Hg) and CVP (from 15 to 30 mm Hg). Appropriate antibiotics were administered intravenously according to the possible source of infection for patients with sepsis syndrome in the ED.

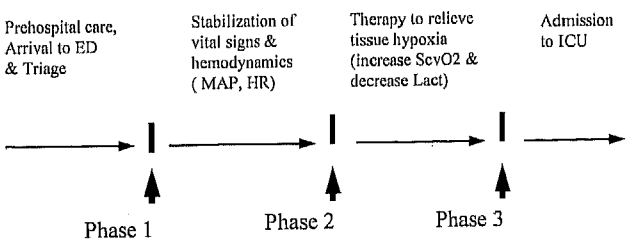

FIGURE 1. The three phases of the study of critically ill patients in the ED: phase 1 denotes the time of arrival and triage in the ED; phase 2 denotes the stabilization of vital signs and hemodynamics, including MAP and HR; phase 3 denotes further therapy to relieve tissue hypoxia by increasing $ScvO_2$ and decreasing Lact. All patients were admitted to the ICU for further therapy.

TABLE 1. Resuscitation Protocol (Phase 2) and End Points of Therapy (Phase 3) of the Critically Ill in the ED

(1). Inspired O_2 to maintain peripheral pulse oximetry >97%
(2). Endotracheal intubation and mechanical ventilation:
Protection of the airway;
Relief of respiratory distress despite supplementary oxygen;
Necessity of inspired O_2 concentration >60% to maintain arterial saturation >97%;
Increasing arterial P_{CO_2} >60 mm Hg
(3). Blood volume expansion with crystalloid, colloid, and red cell concentrate
Central venous pressure (CVP = 20 mm Hg)
Hemoglobin concentration (10 to 12 g/dL)
(4). Cardioactive and vasoactive drugs depending on the etiology of acute illness
HR (>50 beats/min and <120 beats/min)
MAP (>70 mm Hg and <110 mm Hg)
CVP (>15 mm Hg and <30 mm Hg)
Increase $ScvO_2$ >65% (at phase 3)
Reduce Lact <2.0 mmol/L (at phase 3)

Therapy to Relieve Tissue Hypoxia (Phase 3)

Additional therapy was given if $ScvO_2$ was reduced <65% and/or Lact was elevated >2.0 mmol/L after initial resuscitation and hemodynamic stabilization. Mechanical ventilation, initiation and/or adjustment of the dosage of infusion of cardioactive (dobutamine, intravenous nitroglycerine) and/or vasopressor (dopamine, norepinephrine) medications, and additional administration of fluids or packed red cells were used to increase the $ScvO_2$ and decrease Lact during that phase of treatment (Table 1). Intravenous nitroglycerin (10 to 50 μg/min) was infused to reduce the preload and afterload and its dose was reduced or terminated if MAP decreased to <60 mm Hg. Dobutamine (2.5 to 10 μg/kg/min) infusion was adjusted to increase $ScvO_2$ and its dose was reduced or stopped if tachyrhythmia, HR >120 beats/min, or ST segment changes developed during the infusion. Infusion of dopamine (5 to 20 μg/kg/min) and norepinephrine (0.05 to 0.2 μg/kg/min) were monitored by the MAP and $ScvO_2$ responses and the dosages were reduced or terminated if HR increased to >120 beats/min, MAP increased to >110 mm Hg, or $ScvO_2$ decreased to <50% during the infusion.

Measurements

Measurements of SBP, DBP, MAP (noninvasive inflatable pneumatic cuff), HR (apical auscultation or electrocardiogram [ECG] monitor), respiratory rate, and rectal body temperature were recorded immediately when the patient arrived at the ED (phase 1). Femoral or radial arterial and central venous catheters (Cook Critical Care Inc, Bloomington, IA) were inserted for direct pressure measurements and connected to precalibrated pressure transducers (Sorenson Transpac, Abbot Systems, Bloomington, IA) through a heparinized saline solution flush system during initial resuscitation at phase 2. ECG, arterial and central venous pressures, and pulse oximetry were displayed simultaneously on multichannel bedside monitors (Hewlett-Packard, Sunnyvale, CA). A 7.5F fiberoptic 20-cm triple lumen catheter (Resuscicath; Life Indications, Minneapolis,

MN) was placed in the right atrium through a Touhey Borst introducer (Cook Critical Care Inc, Bloomington, IA) and its position was confirmed radiologically after hemodynamic stabilization. Each fiber-optic catheter was calibrated in vitro (before insertion) and in vivo (after placement) with venous oxyhemoglobin saturation measured by co-oximeter (Co-oximeter 282; Lexington, MA). $ScvO_2$ was measured continuously by American Edwards SAT-Com-2 (Baxter Health Care, Irving, CA). Arterial blood lactic acid concentration was measured by lactic acid oxidase enzymatic assay in duplicate. $ScvO_2$ and Lact were measured in addition to HR, SBP, DBP, MAP, and SI after initial resuscitation and hemodynamic stabilization (phase 2). Repeat measurements were made after additional therapy to reverse tissue hypoxia was completed in the ED (phase 3).

Definitions of Diagnosis

Sepsis was defined by clinical features of respiratory rate >20 breaths/min, HR >90 beats/min, body temperature >38°C or <36°C, white cell count >12,000/μL or <4000/μL and positive bacterial culture from blood and/or site of infection.[6] Pneumonia was confirmed by the presence of lobar consolidation on chest radiography, and positive sputum culture and urosepsis was confirmed by positive bacterial culture $>10^5$ colony-forming units and the presence of leucoesterase positive white cell >20/μL. Acute exacerbation of congestive heart failure (CHF) was defined by previous documentation of a poor left ventricular function (ejection fraction below 30% by echocardiography within 2 months of presentation), gallop rhythm, pulmonary and systemic fluid sequestration, and venous congestion from physical examination and chest radiography and CVP >30 mm Hg.[7] Acute diabetic ketoacidosis was defined by the elevation of blood glucose >400 mg/L, serum betahydroxybutrate >0.4 mmol/L, arterial blood pH <7.3, and the need for intravenous insulin to correct hyperglycemia. Adult respiratory distress syndrome (ARDS) was defined as pulmonary failure requiring mechanical ventilation with inspired oxygen concentration of 40% or higher to maintain arterial oxyhemoglobin saturations of 97%, bilateral diffuse interstitial infiltrate on chest radiographs, and pulmonary capillary wedge pressure <18 mm Hg measured with pulmonary artery catheter in the ICU.[8]

Statistical Analysis

The data collected satisfied the criteria for parametric testing and some variables required logarithmic transformation before analysis. Analysis of variance (ANOVA) and Tukey's intervals were used for multiple comparisons at different times between different groups. Fisher's exact test was used to analyze the distribution of patients between different groups. The sample size was sufficient for the experimental design ($\beta = 0.1$) and statistical significance (or α) was accepted at $P < .05$.

RESULTS

A total of 36 patients were studied and were allocated immediate treatment triage priority on arrival at the ED. All 36 patients were admitted to the medical ICU for continued therapy. The mean time from arrival at the ED until admission to the ICU, ie, from phase 1 to phase 3 (Figure 1) was 364 ± 185 minutes (mean ± SD) and the range was between 90 minutes and 810 minutes. Age, gender, diagnosis, and therapy completed in the ED are listed in Table 2. The spectrum of critical illness consisted of the following: sepsis syndrome related to pneumonia in 12 patients, urosepsis in 8, aortic prosthetic graft infection in 1, and sepsis from decubitus ulcer in 1 paraplegic patient. Acute cardiac failure was related to CHF in 10 patients, after pulmonary embolism in 1 patient and after non-Q infarction and septicemia in 1 patient. Three patients presented with acute diabetic ketoacidosis and 1 patient with an acute upper gastrointestinal bleeding. Fifteen patients required endotracheal intubation and mechanical ventilation, and the reminder required supplemental inspired oxygen to maintain pulse oximetry at 97% or higher. Twenty-eight patients required administration of one or more cardioactive and/or vasoactive medications during therapy in the ED.

Mean body temperature was 37.0 ± 1.6°C and respiratory rate was 28 ± 10 breaths/min at triage or phase 1. Initial resuscitation increased SBP and MAP at phase 2 and additional therapy at phase 3 produced no additional significant increases at phase 3 (Figure 2 and Table 3). HR, DBP, and SI did not change significantly throughout the entire time course of the study, ie, phase 1 to phase 3 (Figure 2 and Table 3). Some patients failed to reach the predefined criteria of hemodynamic stability with the number of patients with HR >120 beats/min remaining similar at all phases of the study; however, the number of patients who had SBP <100 mm Hg or MAP <70 mm Hg were significantly reduced at phases 2 and 3, (Table 3). The number of patients with SI ≥0.9 remained elevated at phase 2 and a significant reduction was only seen at phase 3. A large proportion of patients (31 out of 36) were found to have $ScvO_2$ <65% and/or Lact >2.0 mmol/L at phase 2 and required additional therapy. Eight patients required mechanical ventilation and skeletal muscle paralysis that increased $ScvO_2$ and decreased Lact at phase 3. Packed red cell concentrate was given to two patients as an additional therapy at phase 3. Twelve patients with acute cardiac failure required additional therapy with intravenous nitroglycerin, dobutamine, dopamine, and/or norepinephrine to increase $ScvO_2$ and reduce Lact at phase 3. Nine patients benefited from additional fluid infusion and adjustment of vasoactive and cardioactive support already initiated at phase 2 to increase $ScvO_2$ and reduce Lact. Additional therapeutic interventions did not produce any significant change in HR, MAP, and SI, although simultaneous significant increases in $ScvO_2$ and decreases in Lact were seen at phase 3 (Figure 2). The proportion of patients with Lact >2.0 mmol/L was significantly reduced before the proportion of patients with $ScvO_2$ <65% at phase 3 (Table 3).

Patients were divided into two groups according to the SI at each phase of treatment (Table 4). Patients with SI ≥0.9 had higher HR and lower SBP, DBP, and MAP than patients with SI <0.9 at all phases of the study. Patients with SI <0.9 had stable HR, SBP, DBP, and MAP at phases 1 and 2 and did not change significantly at phase 3 although there was simultaneous increase in $ScvO_2$ and decrease in Lact at phase 3 (Table 4). For patients with SI ≥0.9, SBP and MAP

TABLE 2. Patient Characteristics, Diagnosis, and Therapy in the ED

No.	Age (yr)	Sex	Diagnosis	Therapy	Outcome
1	30	F	Pneumonia	MV + F + Antib + Dopa	S
2	69	F	Urosepsis	MV + F + Antib + Dobu + Dopa	S
3	90	M	Pneumonia	O_2 + F + Antib + Dopa	S
4	67	M	Pneumonia	O_2 + F + Antib + Dopa	S
5	58	F	CHF	MV + Lasix + morphine + NTG + F	S
6	56	M	Septicemia + non-Q AMI	MV + F + NTG + Dopa + Antib	S
7	64	F	Pneumonia	O_2 + F + Antib	S
8	85	F	CHF + Urosepsis	O_2 + F + Antib + Dopa + Dobut	S
9	76	M	Pneumonia	O_2 + F + Antib	S
10	41	F	Septicemia, decubitus ulcer	O_2 + F + Antib	S
11	43	F	Urosepsis	O_2 + F + Antib + PRBC	S
12	60	F	Aortic prosthetic graft infection	MV + F + PRBC + Dobu + Levophed	NS
13	55	M	DKA	O_2 + F + Insulin	S
14	70	M	Urosepsis, acute renal failure	O_2 + F + Antib + Dopa	S
15	18	M	DKA, septicemia	MV + F + Antib + Levophed + Dopa	NS
16	60	M	CHF	MV + Lasix + Dobu + NTG + Dopa	NS
17	52	M	COPD, pneumonia	MV + F + Antib + Dopa	NS
18	57	F	DKA	O_2 + F + Insulin	S
19	79	F	CHF	O_2 + Lasix + morphine + Dobu + F + Levophed	S
20	62	M	Urosepsis	O_2 + F + Dopa + Antib	S
21	47	M	Pneumonia, AIDS	O_2 + F + Levophed + Antib	S
22	76	M	Urosepsis	MV + F + Antib + Dobu + Levophed	S
23	60	M	Pulmonary embolism	O_2 + F + Dopa + heparin	S
24	73	M	Pneumonia + ARDS	MV + F + Antib + Dopa	S
25	65	F	Aspiration pneumonia + ARDS	MV + F + Antib + Dopa	S
26	49	M	Pneumonia + ARDS	MV + F + Antib + Dopa	NS
27	47	M	Pneumonia + ARDS	MV + F + Antib	S
28	51	M	CHF + urosepsis	O_2 + F + Antib + Dobu + Levophed	S
29	61	M	CHF	MV + Lasix + NTG + Dobu + F	S
30	83	M	CHF	O_2 + Lasix + NTG + Dobu + F	S
31	72	F	CHF	O_2 + Lasix + NTG + Dobu + F	S
32	64	F	CHF	MV + Lasix + NTG + Dobu + F	S
33	81	M	GI bleeding	O_2 + F + PRBC	S
34	80	M	Pneumonia	O_2 + F + Antib + Dopa	S
35	74	M	Urosepsis	O_2 + F + Antib + Dopa	S
36	46	M	CHF	O_2 + Lasix + NTG + Dobu + F	S

ABBREVIATIONS: F, female; M, male; S, survivor; NS, nonsurvivor; MV, mechanical ventilation; F (under "Therapy"), intravenous fluids; Dopa, Dopamine; Antib, antibiotics; Dobu, dobutamine; O_2, supplemental inspired oxygen with spontaneous breathing; NTG, intravenous nitroglycerine; AMI, acute myocardial infarction; PRBC, packed red blood cell infusion; Levophed (Sanofi Winthrop, New York, NY), norepinephrine; Lasix (Hoechst-Roussel, Somerville, NJ), furosemide; CHF, congestive heart failure; DKA, diabetic ketoacidosis; COPD, chronic obstructive pulmonary disease; AIDS, acquired immunodeficiency syndrome; ARDS, adult respiratory distress syndrome.

were increased at phase 2 and additional therapy produced no further significant changes in HR, SBP, DBP, MAP, and SI, although $ScvO_2$ was increased and Lact was decreased at phase 3 (Table 4). Although there was a significantly higher proportion of patients who failed to reach predefined goals of hemodynamic stability with HR >120 beats/min, SBP <100 mm Hg, and MAP <70 mm Hg in the group with SI ≥0.9 than there was in the group with SI <0.9 at phases 1 and 2, there was a similar proportion of patients (approximately 75%) with abnormally reduced $ScvO_2$ <65% or elevated Lact >2 mmol/L in both groups at phase 2 (Table 5). Additional therapy reduced the proportion of patients with Lact >2 mmol/L before a significant decrease of the proportion of patients with $ScvO_2$ <65% in both groups (ie, group SI ≥0.9 and group SI < 0.9) at phase 3 (Table 5).

Twelve patients with acute cardiac failure were examined for simultaneous responses of the HR, MAP, SI, $ScvO_2$, and Lact during additional therapy (Figure 3). It was apparent that a significant increase in $ScvO_2$ and a decrease in Lact were not associated with any significant changes in HR, MAP, or SI from phase 2 to phase 3.

There were five nonsurvivors (14% mortality) in that group of critically ill patients. Patient no. 12 presented with sepsis syndrome from an infection of a thoraco-abdominal aortic prosthetic graft and she was considered inoperable. Her $ScvO_2$ remained below 50% and Lact above 12.4 mmol/L after medical therapy, and she died 12 hours later. Patient no. 15 failed to respond to therapy, and Lact increased from 2.5 to 8 mmol/L in the ED; this patient died from multiple organ failure 2 days later. Patient no. 16 had an $ScvO_2$ of 40% and subsequent therapy failed to increase $ScvO_2$ above 45%; he died 3 days later with acute hepatic and renal failure. Patient no. 17 had end-stage chronic obstructive pulmonary disease and therapy was withdrawn at the family's request later in the ICU. Patient no. 26, who had a history of intravenous drug abuse, had Lact of 11.7

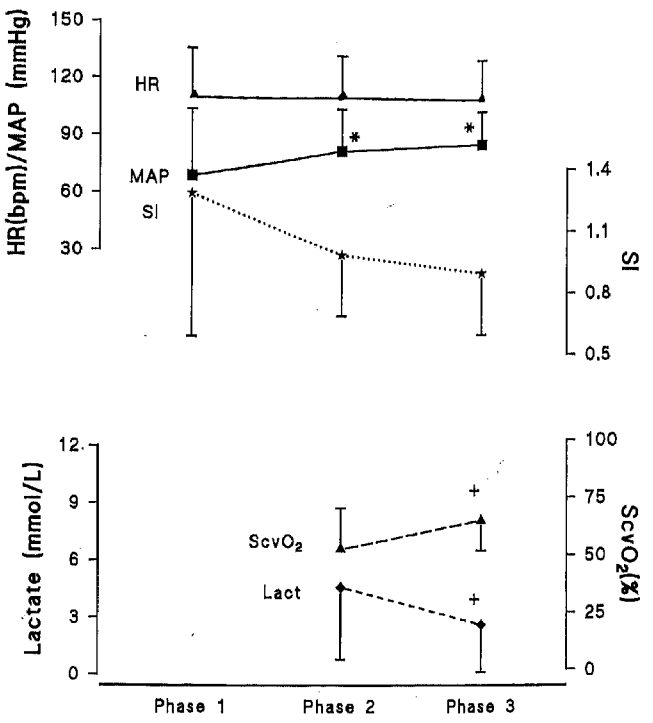

FIGURE 2. HR, MAP, SI, $ScvO_2$, and Lact in 36 critically ill patients at triage (phase 1), after initial resuscitation (phase 2), and completion of therapy (phase 3) in the ED. Values shown are means and error bars represent one standard deviation. *, $P < .05$ *vs* phase 1; +, $P < .05$ *vs* phase 3.

mmol/L and remained above 4.7 mmol/L after therapy. He died from multiple organ failure in the ICU.

DISCUSSION

Significant correlation and similar trend between $ScvO_2$ (which is measured at the right atrium) and mixed venous blood SvO_2 (which is measured in the pulmonary artery) have been shown during therapeutic interventions and resuscitation of critically ill patients.[4] An augmentation of systemic oxygen delivery and a reduction in systemic oxygen demands and consumption have been shown to increase $ScvO_2$ and SvO_2 and restore systemic oxygenation.

TABLE 3. Incidence of Abnormal Hemodynamics and Oxygenation at Triage (Phase 1), After Initial Resuscitation (Phase 2), and Completion of Therapy (Phase 3)

	Phase 1 (n = 36)	Phase 2 (n = 36)	Phase 3 (n = 36)
SBP (mm Hg)	103 ± 39	118 ± 29*	121 ± 27*
DBP (mm Hg)	53 ± 35	63 ± 22	65 ± 14
HR >120 beats/min	13	11	11
SBP <100 mm Hg	20	12*	9*
MAP <70 mm Hg	18	10*	7*
SI ≥0.9	22	20	14*
$ScvO_2$ <65%	—	25	21
Lactate >2.0 mmol/L	—	27	13†

NOTE: Values shown are absolute numbers of patients.
*$P < .05$ *vs* phase 1.
†$P < .05$ *vs* phase 2.

Prolonged placement of indwelling central venous catheters in the right atrium is generally not recommended because of the potential risk of injury to atrial wall or rupture. However, the placement of a right atrial fiber-optic catheter to measure $ScvO_2$ during resuscitation and hemodynamic stabilization has not been associated with harmful side effects in critically ill patients.[1,4] Previous work indicated that abnormal reduction of $ScvO_2$ and the elevation of Lact and SI persisted after resuscitation and stabilization of HR, MAP, and CVP in critically ill patients in the ED.[1] The present study examined in detail simultaneous responses of SBP, DBP, MAP, HR, SI, $ScvO_2$, and Lact to initial resuscitation and then additional therapeutic interventions to restore systemic oxygenation in critically ill patients in the ED. The time course of the study in the ED was divided into three phases to detect differences in the trend of the measured variables over time. Patients arrived at the ED and were allocated triage priority for treatment after measurement of their vital signs and evaluation of other clinical features of the acute illness (phase 1). Initial resuscitation and stabilization of vital signs, eg, HR, SBP, DBP, MAP, etc, was followed by the measurement of $ScvO_2$ and Lact (phase 2). Additional therapy was initiated to correct abnormally reduced $ScvO_2$ (<65%) and/or elevated Lact (>2 mmol/L) and responses of all variables were evaluated simultaneously at phase 3. The measurements of systemic oxygen delivery and consumption are *direct* markers of adequacy of systemic oxygenation and can be difficult to measure during resuscitation in the ED. In contrast, reduced $ScvO_2$ and/or elevated Lact are *indirect* markers of deficient systemic oxygenation and hypoperfusion, which explains the rationale for utilizing them to guide additional therapy in phase 3. Several clinical studies have shown that early and rapid relief of tissue hypoxia and restoring systemic oxygen delivery and consumption reduced the incidence of morbidity and mortality in critically ill patients.[9-11]

The spectrum of critical illness consisted of medical emergencies, eg, sepsis, cardiac failure, diabetic ketoacidosis, gastrointestinal bleeding, and pulmonary embolism. The categories of trauma and acute surgical emergencies were excluded from this particular study because these patients often require rapid transfer to the operating room for operative treatment of the underlying pathology after initial resuscitation. Early operative intervention is an essential component to optimize systemic oxygenation and relieve tissue hypoxia after hemodynamic stabilization in that particular group of patients.[12]

Initial resuscitation included mechanical ventilation or supplemental O_2, fluids, vasopressors, intravenous frusemide, morphine, and/or nitroglycerin to achieve hemodynamic stability at phase 2. Some patients failed to reach the predefined goals of HR <120 beats/min and MAP >70 mm Hg after initial resuscitation at phase 2 and additional therapy at phase 3. In fact, there were no significant changes in the mean HR over the entire time course of the study or the proportion of patients with HR >120 beats/min even after additional therapy to restore systemic oxygenation at phase 3. The beneficial effects of additional therapy and the improvement noted in $ScvO_2$ and Lact were not associated with any appreciable change in HR, SBP, DBP, or MAP between phase 2 and phase 3.

TABLE 4. Hemodynamics and Oxygenation in Patients With SI <0.9 Versus Patients With SI ≥0.9 at Triage (Phase 1), After Initial Resuscitation (Phase 2), and After Completion of Therapy (Phase 3) in the ED

	Phase 1		Phase 2		Phase 3	
	SI <0.9 (n = 14)	SI ≥0.9 (n = 22)	SI <0.9 (n = 16)	SI ≥0.9 (n = 20)	SI <0.9 (n = 22)	SI ≥0.9 (n = 14)
Age (yr)	63 ± 16	61 ± 15	64 ± 15	61 ± 16	64 ± 14	58 ± 17
HR (beats/min)	99 ± 22	117 ± 26*	99 ± 21	118 ± 19*	100 ± 22	116 ± 14*
SBP (mm Hg)	136 ± 32	84 ± 27*	138 ± 23	100 ± 21*†	134 ± 24	101 ± 17*
DBP (mm Hg)	81 ± 23	44 ± 30*	75 ± 11	62 ± 16*	70 ± 14	58 ± 11*
MAP (mm Hg)	94 ± 29	54 ± 27*	96 ± 12	71 ± 22*†	92 ± 15	72 ± 11*
SI	0.7 ± 0.1	1.5 ± 0.7*	0.7 ± 0.1	1.2 ± 0.2*	0.7 ± 0.1	1.2 ± 0.2*
$ScvO_2$ (%)	—	—	54 ± 9	52 ± 12	65 ± 12‡	67 ± 14‡
Lactate (mmol/L)	—	—	3.8 ± 3.4	5.6 ± 3.7	2.2 ± 1.8‡	3.1 ± 3.0‡

NOTE: Values shown are means ± SD.
*$P < .05$ SI ≥ 0.9 *vs* SI <0.9.
†$P < .05$ phase 2 *vs* phase 1.
‡$P < .05$ phase 3 *vs* phase 2.

Thirty-one patients (86%) had evidence of deficient systemic oxygenation and hypoperfusion ($ScvO_2$ <65% and/or Lact >2.0 mmol/L) at phase 2 and required additional resuscitation. Mechanical ventilation and skeletal muscle paralysis were sufficient to reduce systemic oxygen consumption and demands and, therefore, increased $ScvO_2$ and decreased Lact in eight patients at phase 3. The oxygen demands of the respiratory muscles to maintain spontaneous breathing were considerable to decrease $ScvO_2$ and increase anaerobic lactate production.

Administration of inotropes (eg, dobutamine), load reducing agents (eg, nitroglycerin) and plasma volume expansion with fluids to increase cardiac output and systemic oxygen delivery successfully increased $ScvO_2$ and decreased Lact at phase 3. The HR, MAP, and SI failed to reflect persistent hypoxia and hypoperfusion as shown by abnormally low $ScvO_2$ (mean of 40%) and elevated Lact (mean of 3.8 mmol/L) in 12 patients with acute cardiac failure at phase 2 (Figure 3). Further treatment with dobutamine, nitroglycerin, and in some cases, infusion of fluids were required to increase $ScvO_2$ and decrease Lact. The lack of appreciable response in HR, MAP, and SI with concurrent significant increases in $ScvO_2$ and decreases in Lact was evident after additional therapy in acute cardiac failure. The measurements of HR, MAP, and SI poorly predict the need for continued resuscitation and the effectiveness of treatment to correct deficient systemic oxygenation in this clinical situation.[7] Indirect markers of systemic oxygen transport (eg, $ScvO_2$ and Lact) rather than HR, MAP, or SI should be utilized to characterize the severity of global ischemia and to decide on the use of inotropic support and unloading medications in patients with acute cardiac failure and CHF.[7,13]

Packed red cell transfusion was administered to three patients to increase their arterial oxygen carrying capacity and systemic oxygen delivery and thereby reverse tissue hypoxia and inadequate systemic oxygenation. Two of the three patients required red cell transfusion after hemodynamic stabilization at phase 2. Hemodilution after fluid administration was a factor to reduce the arterial oxygen carrying capacity and $ScvO_2$ in these two patients. Although therapy was given to increase $ScvO_2$ and decrease Lact, the proportion of patients with Lact >2 mmol/L was reduced before an apparent reduction in the proportion of patients with $ScvO_2$ <65% at phase 3. Rapid elimination of Lact indicated relief of tissue hypoxia and cessation of anaerobic metabolism and Lact production in addition to augmented oxygenation of the liver and kidneys responsible for metabolism of Lact in these patients.[14] Restoration of systemic oxygenation reverses anaerobic metabolism and repays systemic oxygen debt (and reduces Lact) initially and

TABLE 5. Incidence of Abnormal Hemodynamics and Oxygenation in Patients With SI <0.9 Versus Patients With SI ≥0.9 at Triage (Phase 1), After Initial Resuscitation (Phase 2), and After Completion of Therapy (Phase 3) in the ED

	Phase 1		Phase 2		Phase 3	
	SI <0.9 (n = 14)	SI ≥0.9 (n = 22)	SI <0.9 (n = 16)	SI ≥0.9 (n = 20)	SI <0.9 (n = 22)	SI ≥0.9 (n = 14)
HR >120 beats/min	3	10*	3	8*	5	6*
SBP <100 mm Hg	2	18*	0	12*	1	8*
MAP <70 mm Hg	2	16*	0	10*	2	5*
$ScvO_2$ <65%	—	—	12	13	14	7
Lactate >2.0 mmol/L	—	—	10	17	5†	8†

NOTE: Values shown are absolute numbers of patients.
*$P < .05$ SI ≥0.9 *vs* SI <0.9.
†$P < .05$ phase 3 *vs* phase 2.

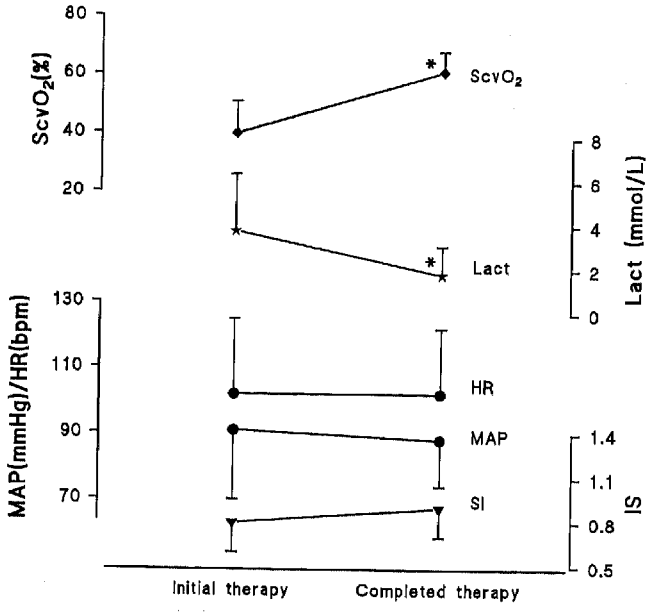

FIGURE 3. HR, MAP, SI, $ScvO_2$, and Lact after initial stabilization (phase 2) and after completion of therapy (phase 3) in 12 patients presenting with acute cardiac failure. Values plotted are means and error bars represent one standard deviation. *, $P < .05$ phase 2 *vs* phase 3.

replenishes systemic venous oxyhemoglobin store (and increases $ScvO_2$) later.

Previous work indicated that an elevation of the SI coincided with deterioration of left ventricular mechanical performance and was related to multiple factors in critically ill patients.[15] A significant proportion (approximately 75%) of critically ill patients with SI ≥0.9 and SI <0.9 had deficient systemic oxygenation (ie, reduced $ScvO_2$ <65% and Lact >2 mmol/L), which indicated that the measurement of SI at a single time point could not discriminate between patients with persistent global hypoxia. This finding is consistent with the low sensitivity of the SI ≥0.9 to identify critically ill patients and the poor correlations between SI and systemic oxygen transport variables described in previous studies.[5,15] Although the SI remained abnormally elevated during the entire time course of the study, additional therapy to restore systemic oxygenation reduced the proportion of patients with SI ≥0.9 from 56% at phase 2 to 36% at phase 3 (Figure 2). An improvement of myocardial oxygenation and left ventricular mechanical performance in some patients may explain the reduction in proportion of patients with elevated SI ≥0.9. It seems that the deterioration of left ventricular mechanical performance and concurrent elevation of the SI ≥0.9 appear at a later time after deficient systemic oxygenation is already established and cumulative buildup of myocardial hypoxic-ischemic insult, and before the onset of hemodynamic instability and hypotension in critically ill patients.[15,16]

All thirty-six patients received therapy to increase $ScvO_2$ and decrease Lact in the ED that was continued in the ICU. All patients enrolled in that study and who required additional therapy to increase $ScvO_2$ >65% and decrease Lact <2 mmol/L) did not suffer any adverse effects from either invasive monitoring or the administration of cardioactive and vasoactive medications in the ED. Although the overall mortality was low (14%) in the current study, it was difficult to confirm the benefits of early detection and correction of inadequate systemic oxygenation in the ED because of the lack of a control group. However, it was evident that all nonsurvivors failed to show decreases in Lact and/or increases in $ScvO_2$ after additional therapy during the time of the study compared with survivors who responded to additional therapy with an increase in $ScvO_2$ and a decrease in Lact. This finding by itself can be considered indirect evidence to support the notion that failure to detect and correct tissue hypoxia in the ED can jeopardize the final outcome in critically ill patients. Other randomized control studies have shown conclusively that therapeutic interventions to relieve tissue hypoxia and maximize oxygen delivery early in the course of an acute critical illness improved the outcome in critically ill patients in the ICU.[9-11]

The present study had several limitations. Trauma and acute surgical emergencies were excluded because resuscitation and hemodynamic stabilization (phase 2) could be achieved in the ED; however, subsequent therapy to relieve tissue hypoxia and restore adequate systemic oxygenation (phase 3) cannot be effectively achieved without rapid and appropriate operative treatment of the underlying pathology.[16] $ScvO_2$ (measured in the right atrium) can be unreliable to detect regional or organ-specific hypoxia and can misrepresent the balance between systemic oxygen delivery and oxygen demands in specific clinical conditions, eg, trauma, sepsis, postcardiopulmonary resuscitation, hypothermia, and established multiple organ failure.[17] Alternative markers of systemic oxygenation, eg, Lact, the relationship between oxygen delivery and consumption, or organ-specific oxygenation, eg, gastric tonometry, have to be evaluated simultaneously to overcome the aforementioned limitations. Finally, although the lack of a control group may be a drawback to the current study, it is highly suggestive that early detection and correction of tissue hypoxia ($ScvO_2$ <65% or Lact >2 mmol/L) in the ED can only have a favorable impact on the outcome of critically ill patients. Future studies should address the cost-benefit and feasibility of initiation of additional monitoring of global and regional oxygenation and therapy to repay oxygen debt in the ED. New therapeutic interventions also need to be developed to reverse tissue hypoxia in those critically ill patients who are unresponsive or refractory to current therapy regimen.

CONCLUSIONS

Initial resuscitation efforts do not always relieve tissue hypoxia and additional therapy is required in the majority of critically ill patients treated in the ED to restore adequate systemic oxygenation and perfusion. Beneficial effects of additional therapy to increase $ScvO_2$ and decrease Lact may not be associated with any substantial responses in HR, SBP, DBP, MAP, or SI. The measurement of $ScvO_2$ and Lact can be utilized to guide additional therapy to improve the care and outcome of critically ill patients in the ED.

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