CHEST

Original Research

SEPTIC SHOCK

Translating Research to Clinical Practice*

A 1-Year Experience With Implementing Early Goal-Directed Therapy for Septic Shock in the Emergency Department*

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Objective: **Early goal-directed therapy (EGDT) has been shown to decrease mortality in patients with severe sepsis and septic shock. Consensus guidelines now advocate EGDT for the first 6 h of sepsis resuscitation. However, EGDT has not yet been widely adopted in practice. A need for effective collaboration between emergency medicine and critical care medicine services has been identified as an obstacle for implementation. We aimed to determine if EGDT end points could reliably be achieved in real-world clinical practice.**

Methods: **EGDT was implemented as a collaborative emergency medicine/critical care quality improvement initiative. EGDT included the following: IV fluids (IVF) targeting central venous pressure ≥ 8 mm Hg, vasopressors targeting mean arterial pressure ≥ 65 mm Hg, and (if necessary) packed RBCs (PRBCs) and/or dobutamine targeting central venous oxygen saturation ≥ 70%. A retrospective analysis was performed of emergency department (ED) patients with persistent sepsis-induced hypotension (systolic BP < 90 mm Hg despite 1.5 L of IVF) treated with EGDT during the first year of the initiative. Primary outcome measures included successful achievement of EGDT end points and time to achievement. A secondary analysis was performed comparing EGDT cases to historical control cases (nonprotocolized control subjects without invasive monitoring).**

Results: **All end points were achieved in 20 of 22 cases (91%). The median time to reach each end point was ≤ 6 h. In the secondary analysis, patients (n = 38; EGDT, n = 22; pre-EGDT, n = 16) had similar age, do-not-resuscitate status, severity scores, hypotension duration, and vasopressor requirement (p = not significant). In the ED, EGDT used more IVF and included PRBC/dobutamine utilization, without any impact on the overall use of these therapies through the first 24 h in the ICU. EGDT was associated with decreased ICU pulmonary artery catheter (PAC) utilization (9.1% vs 43.7%, p = 0.01).**

Conclusions: **With effective emergency medicine/critical care collaboration, we demonstrate that EGDT end points can reliably be achieved in real-world sepsis resuscitation. ED-based EGDT appears to decrease ICU PAC utilization.** ***(CHEST 2006; 129:225–232)***

Key words: diffusion of innovation; sepsis; septic shock; shock

Abbreviations: APACHE = acute physiology and chronic health evaluation; CVP = central venous pressure; ED = emergency department; EGDT = early goal-directed therapy; IVF = IV fluid; LOS = length of stay; MAP = mean arterial pressure; MEDS = Mortality in Emergency Department Sepsis; PAC = pulmonary artery catheter; PRBC = packed RBC; $Scvo_2$ = central venous oxygen saturation

Early goal-directed therapy (EGDT) is a research innovation that has been shown to reduce mortality in patients with severe sepsis and septic shock.[1] As described by Rivers et al,[1] EGDT is a sepsis cardiovascular support protocol aimed at early hemodynamic optimization. The protocol is initiated as soon as sepsis-induced hypoperfusion is identified and targets end points of resuscitation derived from hemodynamic

P06-0425

monitoring (central venous pressure [CVP], mean arterial pressure [MAP], and central venous oxygen saturation [$Scvo_2$]). In a study of 263 patients, EGDT was associated with a 16% absolute risk reduction for in-hospital mortality, which to date is the largest mortality benefit demonstrated in a sepsis randomized controlled trial. Current consensus recommendations[2] now advocate EGDT as best practice for the first 6 h of severe sepsis resuscitation. However, EGDT has not yet been widely adopted in practice. We hypothesized that effective collaboration between emergency medicine and critical care services could facilitate successful implementation of EGDT.

As part of a collaborative emergency medicine/critical care quality improvement initiative, our institution implemented EGDT in 2004. Like most US emergency departments (EDs), our ED did not use any protocolized resuscitation or invasive hemodynamic monitoring prior to EGDT implementation. The primary aim of this study was to determine if EGDT end points could reliably be achieved in real-world clinical practice. In addition, because the "standard care" group (*ie*, control subjects) in the original EGDT study was a concurrent group of patients who also received protocolized care and limited invasive monitoring in the ED (which is not typical for current practices in most US EDs), a secondary aim of this study was to determine the impact of EGDT implementation on resource utilization compared to nonprotocolized historical controls with no invasive monitoring.

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There was no source of external funding for this study. The authors' institution received an unrestricted educational grant from Edwards Lifesciences for an education program prior to protocol implementation.

Manuscript received May 20, 2005; revision accepted August 5, 2005.

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Materials and Methods

Study Design and Setting

This was a retrospective cohort study at an urban academic medical center (Cooper University Hospital, Camden, NJ), with an ED volume of 48,000 annual patient visits. The institution has an emergency medicine residency program and a multispecialty critical care medicine fellowship program.

Cooper University Hospital adopted EGDT as a best practice model for sepsis resuscitation on January 1, 2004. The EGDT program at Cooper University Hospital is a collaborative effort in which the emergency medicine clinicians are responsible for patient identification and initiation of the protocol in the ED, and the critical care clinicians are responsible for ensuring that all end points of resuscitation are achieved. Our EGDT protocol is an adaptation of the protocol by Rivers et al[1] (Fig 1). When a patient is identified, crystalloid resuscitation is continued while an oximetric central venous catheter (Pre-sep; Edwards Lifesciences; Irvine, CA) is inserted into the superior vena cava via the internal jugular or subclavian technique. Our protocol differs slightly from the Rivers et al[1] protocol, in that our monitoring of EGDT end points is continued into the ICU phase of therapy until discontinued based on ICU physician discretion (rather than being discontinued at the end of a predefined time period). Our protocol did not mandate a time frame for achievement of each end point, and while executing the protocol our ED and ICU clinicians had no indication that the time to successful achievement of the end points would be tracked.

A faculty physician with expertise in EGDT was available (24 h/d) by pager to answer questions by telephone and provide EGDT support, but no extra clinical staffing (neither nursing nor physician) was provided for bedside EGDT execution. The EGDT protocol was executed by the ED/ICU physicians and nurses as part of their regular duties during a clinical shift. All EGDT cases were initiated in existing ED patient care areas using conventional bedside monitors (DASH 4000; GE Healthcare; Waukesha, WI) and portable $Scvo_2$ monitors (Vigilance; Edwards Lifesciences) that were wheeled to the bedside when needed. Implementing EGDT required no modifications of the ED physical plant.

Subjects

Subjects of the primary analysis included patients with confirmed or suspected sepsis (by consensus definition[3]) and persistent hypotension in the ED (systolic BP < 90 mm Hg despite 1,500 mL of crystalloid IV fluid [IVF]) who were treated with EGDT. These patients were identified using a prospective ED-based quality assurance registry for EGDT that was compiled over the first year of protocol implementation. Patients were determined to have in fact been treated with EGDT if any value for $Scvo_2$ was found in the ED record, regardless of whether or not the end points of EGDT were achieved in the ED (intention-to-treat). Although lactate elevation is also a trigger for EGDT in our protocol (as was done in the original EGDT study[1]), patients without hypotension were excluded from this analysis because we did not routinely check lactate in practice before the EGDT program began, and therefore (in the absence of hypotension) a secondary analysis comparing EGDT to historical controls would not have been possible.

The secondary analysis included a comparison group of nonprotocolized historical control subjects with sepsis (consensus definition[3]) and persistent hypotension in the ED (defined above) admitted from ED to the ICU in the 1 year immediately prior to EGDT implementation. The pre-EGDT group was identified retrospectively utilizing an administrative database

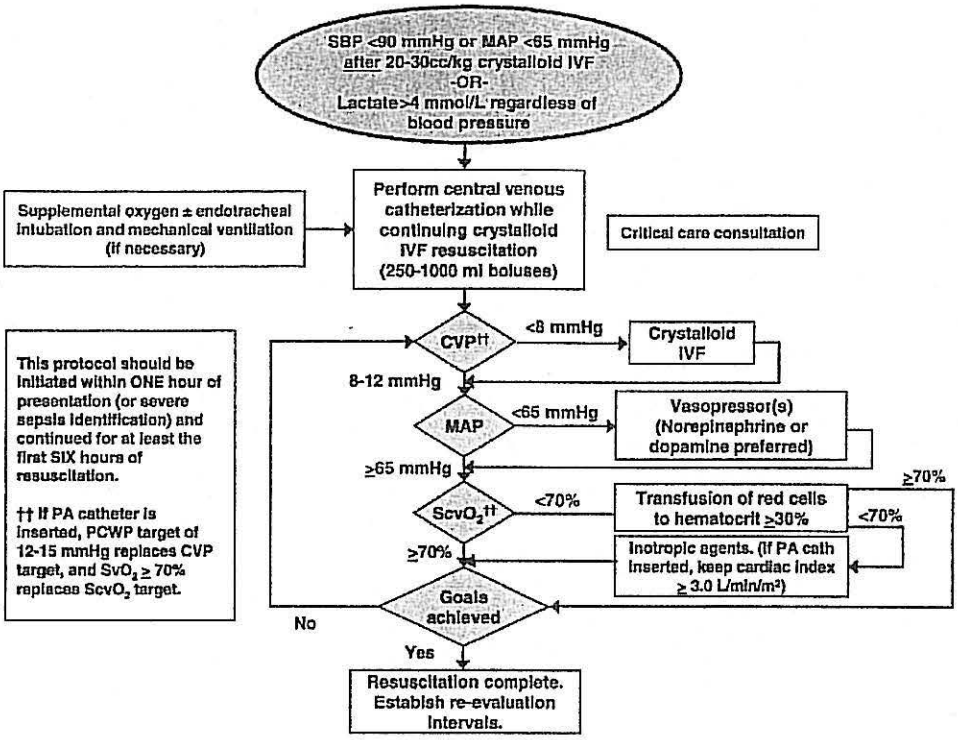

FIGURE 1. The EGDT protocol utilized at Cooper University Hospital (an adaptation of the protocol by Rivers et al[1]). Clinical criteria for triggering the protocol include a clinical suspicion of sepsis plus one of the following: (1) systolic BP (SBP) < 90 mm Hg or MAP < 65 mm Hg (despite a 20 to 30 mL/kg crystalloid IVF bolus), or (2) lactate ≥ 4 mmol/L. IVF is administered to achieve a CVP ≥ 8 mm Hg, vasopressors (preferably norepinephrine or dopamine) are administered as needed to achieve MAP ≥ 65 mm Hg, and PRBCs and/or dobutamine are administered as needed in order to achieve a $Scvo_2$ ≥ 70%. Our protocol differs slightly from the Rivers protocol in that (after initiation in the ED) it is intended to continue into the ICU phase of patient care, where the monitoring device may be changed to a PAC based on individual clinician preference. If a PAC is utilized, a target for pulmonary capillary wedge pressure replaces the target for CVP, and mixed venous oxygen saturation (Svo_2) replaces $Scvo_2$. PA = pulmonary artery; cath = catheter.

specifically designed for the critically ill patient (Project IMPACT; Cerner-Project IMPACT; Bel Air, MD).

Data Collection

Four reviewers retrospectively abstracted data (including physiologic parameters, resource utilization, timing of therapies, and outcomes) from the ED and ICU course. An analysis of interobserver agreement for both categorical and continuous variables was performed. Time to achievement of each EGDT end point was defined as the time from documented criteria for triggering the EGDT protocol until the time of a documented value in the medical record that met or exceeded the target values for CVP, MAP, or $Scvo_2$. After the secondary analysis was complete, we also performed an analysis of the rate of pulmonary artery catheter (PAC) utilization in sepsis patients admitted to the ICU from non-ED locations during the EGDT time period.

Duration of ED hypotension was classified according to previously published criteria[4] (Table 1). Criteria for acute organ dysfunction at the time of initial ED presentation was calculated according to criteria in Table 1. The Mortality in Emergency Department Sepsis (MEDS) severity score was utilized because MEDS is the only prospectively validated scoring system applicable to the time of initial presentation in the ED setting.[5] The APACHE (acute physiology and chronic health evaluation) II score was based on the worst values over the first 24 h of ICU care.[6] Facilities charges (excluding all physician professional fees) were abstracted from the final hospital billing data for each subject. All data were entered into a dedicated computerized database (Microsoft Access; Microsoft Corporation; Redmond, WA).

Data Analysis

χ^2, Fisher exact, Mann-Whitney *U*, and unpaired *t* tests were used as appropriate, and statistical analysis was performed (StatPlus v. 2.5; Brooks/Cole; Belmont, CA). Interobserver agreement was analyzed with the κ statistic. Our institutional review board approved this study with an exemption from informed consent.

RESULTS

Primary Analysis

Of 45 records identified from the EGDT registry in 2004, 23 records did not meet the criteria for hypotension in the ED (normotensive with lactate elevation), leaving 22 EGDT subjects in the primary analysis. All 22 subjects were admitted from the ED

Table 1—*Methods for Classifying Hypotension Duration and Organ System Dysfunction*

Methods	Requirements
Duration of hypotension*	
Sustained	Systolic BP < 100 mm Hg without recovery (no measurements ≥ 100 mm Hg) for ≥ 60 min
Transient	Systolic BP < 100 mm Hg followed by at least two readings ≥ 100 mm Hg at least 15 min apart and no subsequent readings < 100 mm Hg
Episodic	Systolic BP < 100 mm Hg not categorized as transient or sustained
Criteria for acute organ system dysfunction†	
Cardiovascular	Systolic BP < 90 mm Hg or MAP < 70 mm Hg or vasopressor requirement for at least 1 h despite fluid resuscitation
Pulmonary	PaO_2/fraction of inspired oxygen ≤ 300 or requiring > 5 cm H_2O of positive end-expiratory pressure on the ventilator
Metabolic	Serum lactate greater than normal limits per laboratory (2.0 mmol/L)
Renal	Acute rise in serum creatinine > 1 mg/dL over baseline or ≥ 2 mg/dL in absence of known baseline
CNS	Altered sensorium (not chronic) with a Glasgow coma score < 12 in the absence of a primary neurologic insult or sedation/intubation
Hepatic	Total bilirubin ≥ 2 mg/dL (acute)
Hematologic	Platelet count less than half of baseline or < 100,000/μL or prothrombin time > 1.5 times control (and not anticoagulated)

*From the classifications of Jones et al.[4]

†From Project IMPACT database (Cerner-Project IMPACT; Bel Air, MD). The number of organ dysfunctions (either present or absent for each organ system) was calculated for the time of initial presentation in the ED.

to the ICU service. Patient characteristics for the EGDT group are displayed in the right column of Table 2.

All end points of EGDT were successfully achieved for 20 of 22 EGDT cases. In the remaining two cases, CVP and MAP targets were achieved, but the $ScvO_2$ goal was not achieved at any time. In the first of these two cases, markedly low values for $ScvO_2$ with a hematocrit of 24% prompted packed RBC (PRBC) transfusion in the ED per protocol, which achieved the target value for hematocrit.

Table 2—*Patient Characteristics

Characteristics	Pre-EGDT (n = 16)	EGDT (n = 22)	p Value
Age, yr	66.8 ± 14.3	62.5 ± 16.5	0.41
Gender			
Male	10 (62.5)	14 (63.6)	0.94
Female	6 (37.5)	8 (36.4)	
MEDS score (ED arrival)†	12.9 ± 5.2	13.0 ± 4.6	0.99
Number of organ dysfunctions in ED	2.1 ± 1.1	2.9 ± 1.3	0.05
Initial laboratory values			
Hemoglobin, g/dL	10.2 ± 1.8	11.0 ± 2.5	0.34
Creatinine, mg/dL	2.0 ± 1.4	2.9 ± 2.9	0.28
Prothrombin time, s	15.6 ± 2.2	15.2 ± 7.3	0.84
Platelets, $10^3/\mu L$	202 ± 135	269 ± 139	0.15
Glucose, mg/dL	130 ± 50	153 ± 87	0.37
Duration of ED hypotension, %‡			
Transient	0 (0.0)	0 (0.0)	0.99
Episodic	4 (25.0)	2 (9.1)	
Sustained	12 (75.0)	20 (90.9)	
Required vasopressors, %§	10 (62.5)	13 (59.1)	0.83
APACHE II score (ICU)‖	24.7 ± 10.1	23.0 ± 10.5	0.64

*Data are presented as mean ± SD or No. (%).

†From Shapiro et al.[5]

‡According to Jones et al.[4]

§Dopamine ≥ 5 μg/kg/min or any dose of norepinephrine in the ED or first 24 h of ICU course.

‖Based on worst values for the first 24 hours of care in the ICU.

Table 3—*Time to Achievement of EGDT End Points and Other Significant Milestones in EGDT Execution (n = 22)

Variables	Time, h
Central line insertion	
Mean ± SD	2.1 ± 1.7
Median	1.5
Range	1–8
CVP goal achieved†	
Mean ± SD	6.3 ± 3.8
Median	6.0
Range	1–14
MAP goal achieved	
Mean ± SD	5.6 ± 3.2
Median	4.0
Range	2–13
$ScvO_2$ measured	
Mean ± SD	2.4 ± 1.8
Median	2.0
Range	1–8
$ScvO_2$ goal achieved†	
Mean ± SD	6.4 ± 4.0
Median	5.0
Range	2–16

*All times were measured from the time that the patient first met criteria for EGDT.

†Dependent on documentation in the nursing flow sheet or physician note. In some cases, end points may have been achieved earlier and not documented in the chart.

However, dobutamine was not initiated prior to the patient's death (after transfusion failed to normalize $Scvo_2$) because of clinicians' concern over exacerbating tachycardia. In the second case, the $Scvo_2$ goal was not achieved because of the clinicians' lack of adherence to the EGDT protocol. The time required to achieve end points of EGDT (and other milestones in EGDT execution such as central line insertion) are displayed in Table 3. The following median times were observed: central line insertion, 1.5 h; CVP goal, 6.0 h; MAP goal, 4.0 h; $Scvo_2$ measured, 2.0 h; and $Scvo_2$ goal, 5.0 h.

Secondary Analysis

For the secondary analysis, 39 sepsis patients were admitted from the ED to the ICU in 2003. Of these, 23 patients failed to meet the criteria for persistent hypotension in the ED and were excluded, leaving 16 historical controls. A total of 38 subjects (EGDT, n = 22; pre-EGDT, n = 16) were included in the secondary analysis. There was good interobserver agreement for all categorical and continuous variables tested.

Table 2 displays baseline patient characteristics. The EGDT and pre-EGDT subjects were similar with regard to age, gender, advance directive status, and baseline laboratory values (p = not significant for all). The MEDS score in the ED was similar for EGDT (13.0 ± 4.6) compared to pre-EGDT (12.9 ± 5.2) [p = 0.99]. The number of organ dysfunctions were 2.9 ± 1.3 for EGDT and 2.1 ± 1.1 for pre-EGDT (p = 0.05). Duration of hypotension was similar, with 90.9% of EGDT and 75.0% of pre-EGDT subjects (p = 0.99) classified as "sustained"; and the vasopressor requirement was similar, with 59.1% of EGDT and 62.5% of pre-EGDT subjects (p = 0.83) requiring dopamine > 5 μg/kg/min or any dose of norepinephrine. APACHE II scores were similar for EGDT (23.0 ± 10.5) compared to pre-EGDT (24.7 ± 10.1) [p = 0.99].

Table 4 displays data for therapies received and resources utilized, including data for the use of EGDT-dependent therapies (including IVF, vasopressors, PRBCs, and dobutamine) as well as select other therapies advocated by consensus guidelines[2] (including timely administration of antibiotics, low-dose steroids for relative adrenal insufficiency, activated protein C, and prophylaxis against deep venous thrombosis and stress ulcers). Overall rates of central venous catheterization (anytime in the ED or ICU

Table 4—*Therapies Received and Resources Utilized

Variables	Before EGDT (n = 16)	EGDT (n = 22)	p Value
EGDT-dependent therapies			
Crystalloid volume infused, mL			
ED (total)	3,509 ± 2,312	5,685 ± 3,021	0.02
First 24 h in ICU	5,548 ± 4,878	2,752 ± 1,731	0.03
Total (ED plus first 24 h in ICU)	9,057 ± 5,058	7,937 ± 3,435	0.42
Vasopressor use			
In the ED	7 (43.8)	13 (59.1)	0.35
Total (ED or first 24 h in ICU)	10 (62.5)	13 (59.1)	0.83
Received PRBC transfusion			
ED	0 (0.0)	3 (13.6)	0.12
Total (ED or first 24 h in ICU)	7 (43.8)	5 (22.7)	0.17
Received dobutamine			
ED	0 (0.0)	2 (9.1)	0.22
Total (ED or first 24 h in ICU)	2 (12.5)	2 (9.1)	0.94
Other therapies			
Time to antibiotics, h			
Mean	3.0 ± 2.7	2.5 ± 1.7	0.52
Median	2.0	2.0	
Low-dose steroids	5 (31.3)	8 (36.4)	0.74
Activated protein C (for APACHE II score ≥ 25)	1/7 (14.3)	2/6 (33.0)	0.44
Prophylactic therapies			
Deep venous thrombosis	13 (81.3)	19 (86.4)	0.67
Stress ulcer	10 (62.5)	18 (81.8)	0.18
Procedures performed			
Mechanical ventilation			
In the ED	5 (31.2)	3 (13.6)	0.19
Total (ED or any time in ICU course)	8 (50.0)	7 (31.8)	0.26
Central venous catheterization ED or any time in ICU course	15 (93.8)	22 (100)	0.42
Pulmonary artery catheterization	7 (43.8)	2 (9.1)	0.01

*Data are presented as mean ± SD or No. (%).

course) were similar (EGDT, 100%; pre-EGDT, 93.8%; p = 0.42). However, PAC utilization in the ICU was significantly lower with EGDT (9.1%) vs pre-EGDT (43.8%) [p = 0.01]. In the analysis of PAC use during the same time frame of EGDT (2004), patients with sepsis who were admitted to the ICU from locations other than the ED received a PAC in 42% of cases.

Table 5 displays data for outcomes. Differences in ED, ICU, and hospital length of stay (LOS) were nonsignificant. The in-hospital mortality rate was 18.2% in the EGDT group, compared to 43.8% for pre-EGDT (p = 0.09). Median facilities charges (excluding physician professional fees) were $82,233 for EGDT and $135,199 for pre-EGDT (p = 0.14)

Discussion

The transfer of research innovations to clinical practice has historically been a slow and complex process.[7–9] This is an issue of high priority because research transfer is one of the major mechanisms by which medical advances can lead to health-care improvement. Early hemodynamic optimization with an EGDT protocol is a research innovation that has been shown to reduce mortality in severe sepsis and septic shock[1] and is now recommended for use by international consensus.[2] The relatively early commitment to EGDT distinguishes Cooper University Hospital emergency medicine and critical care clinicians as "early adopters" in the model of dissemination of research innovations described by Rogers[10] and Berwick.[7]

Because implementing EGDT in the ED may be challenging, an important practical question for EGDT implementation has been "Can it be done?" Adoption of EGDT at our institution was notable because of the infrastructure required (or not required) for the implementation process. First, we did not allocate any extra clinical staffing (neither nurse nor physician coverage) for the purposes of EGDT execution. Second, at baseline our ED had no special critical care capability beyond what could be found in a conventional ED prior to beginning the EGDT program, and no special modifications of the ED physical plant were required. Third, and most importantly, we relied on a close collaboration between clinicians from emergency medicine and critical care to facilitate the process of change.

The primary aim of this study was to determine if EGDT end points could reliably be achieved in real-world clinical practice. We found that all EGDT end points (CVP, MAP, and $ScvO_2$) were successfully achieved in 20 of 22 EGDT cases (91%). The median times to achievement of each end point were ≤ 6 h. We believe that the times to successful end point achievement in this study reflect what can realistically be expected in the first year of EGDT implementation, and could be reasonably extrapolated to most academic centers. Our data demonstrates that EGDT is not just a research innovation but also a viable clinical practice parameter that can be successfully built into the armamentarium of severe sepsis care for the ED.

The secondary aim of our study was to measure the effect of EGDT implementation on resource

Table 5—*Outcomes*

Variables	Pre-EDGT (n = 16)	EGDT (n = 22)	p Value
ED LOS, h			
Mean ± SD	9.0 ± 6.0	13.9 ± 10.3	0.13
Range	(2–36)	(3–37)	
ICU LOS, d			
All patients			
Median	4.2	1.8	0.12
Range	(0.5–14.3)	(0.0–34.9)	
Survivors only			
Median	2.7	1.8	0.62
Range	(0.5–7.7)	(0.0–34.9)	
Hospital LOS, d			
All patients			
Median	13.0	9.0	0.12
Range	(2–54)	(1–50)	
Survivors only			
Median	13.0	9.0	0.10
Range	(6–54)	(3–50)	
In-hospital mortality, No. (%)	7 (43.8)	4 (18.2)	0.09
Median facilities charge, US$*	135,199	82,233	0.14
Range	(26,456–611,843)	(24,836–729,448)	

*Excluding all physician professional fees.

utilization outside of the confines of a randomized controlled trial. We observed that EGDT utilized more IVF and also incorporated the use of PRBCs/dobutamine in the ED without any significant impact on the overall use of these therapies through 24 h in the ICU. This suggests that the EGDT protocol may not actually increase IVF, PRBC, or inotrope use overall, but may prompt earlier administration (which may be beneficial given the fact that the efficacy of hemodynamic optimization is believed to be time sensitive).[11,12]

It should be noted, however, that apparent similarities in the overall use of these therapies through the first 24 h in the ICU does not exclude the distinct possibility that significant EGDT-specific modifications of therapy are still occurring for individual patients. In contrast to studies in the 1990s that targeted supranormal oxygen delivery, EGDT was designed to pinpoint and normalize specific physiologic derangements (*ie*, CVP, MAP, and $Scv\overline{O}_2$).[1] In this way, the goal-directed approach only gives each individual patient what he or she specifically needs in order to normalize these parameters, and the specific parameters that require normalization will differ from patient to patient. That is why pooled data from a series of patients may fail to identify a significant increase for any single resuscitative measure, but critically important modifications of therapy could still be occurring for patients on an individual basis.

Despite the fact that few patients received PRBCs and/or inotropes per protocol in the ED phase of therapy, this does not indicate that these elements of the EGDT protocol are any less crucial than others, because early administration of PRBCs and/or inotropes may have been critically important for the minority of patients who required them (as identified by low $Scv\overline{O}_2$). It should also be noted that prior to EGDT implementation, no patients received PRBCs or dobutamine in the ED. The transfusion of PRBCs (and concern over potential deleterious effects of blood transfusions if widely adopted) has been one of the most controversial elements of the EGDT study since its publication.[13] It is notable that the overall use of PRBCs from the ED through the first 24 h in the ICU was not elevated (in fact, numerically lower) in the EGDT group despite being initiated earlier. Specifically with regard to inotropes, the 9.1% of patients requiring inotropes in the ED in this study is similar to the Rivers et al[1] data in which 13.7% of the EGDT group required inotropes, and it is consistent with an estimated 10% of septic shock patients having myocardial dysfunction as the predominant feature of the hemodynamic profile.[14]

One of the most interesting findings of this study is the impact on PAC utilization. For these patients with sepsis-induced hypotension, the observed rate of PAC utilization was 9.1% in the EGDT group compared to 43.8% in the pre-EGDT group (and 42% for patients admitted to the ICU with sepsis from non-ED locations during the EGDT time period). Our protocol differed from Rivers et al,[1] in that monitoring of the EGDT end points was continued into the ICU phase of therapy. Among the critical care faculty group, we made no effort to dissuade PAC utilization for the EGDT group admitted from the ED. In fact, we deliberately modified the EGDT protocol prior to implementation in order to allow the ICU physicians to change the monitoring device to a PAC based on individual clinician preference (Fig 1). The fact that there was a significantly lower rate of pulmonary artery catheterization (and confirmed by the rate of PAC utilization in sepsis cases originating from non-ED locations) suggests that the ICU clinicians believed that the monitoring parameters provided by EGDT were usually sufficient for these patients. While EGDT appears to have substituted a central venous catheter for the PAC in the cardiovascular support of many EGDT patients, it is notable that EGDT did not significantly increase the overall rate of central venous catheterization, as the rate of central venous catheterization (anytime in the ED or ICU course) in the pre-EGDT group was 93.8% vs 100% with EGDT.

The main limitations of the secondary analysis are the retrospective methodology and the sample size. Other limitations of this study include the following: (1) a possibility that potential subjects were admitted from the ED to the ICU in the pre-EGDT period but were not included because they were classified with admitting diagnoses other than sepsis; and (2) a possibility that potential subjects admitted from the ED to the ICU during the EGDT period were not included because they did not receive EGDT.

The next step in our sepsis quality improvement initiative at Cooper University Hospital will be to streamline the EGDT process, improving the speed and efficiency of bedside protocol execution. We also will be expanding our quality improvement initiative beyond EGDT to encompass all of the elements of the Surviving Sepsis Campaign change "bundles"[9] to include both the 6-h resuscitation bundle as well as the 24-h sepsis management bundle that were created in partnership with the Institute for Healthcare Improvement (Boston, MA) [available at: www.ihi.org/IHI/Topics/CriticalCare/Sepsis/].

Similar to other disease processes such as acute myocardial infarction, trauma, and stroke, the landscape of this disease is now recognized to be part of a time-sensitive continuum of care, and optimal care of patients on that continuum (from ED to ICU) requires multidisciplinary cooperation. One of the

main reasons that we were able to demonstrate successful transfer of this research innovation to clinical practice was a truly collaborative effort between emergency medicine and critical care clinicians at our institution. The multidisciplinary nature of protocolized resuscitation along a continuum of care may make EGDT challenging to implement, but a shared responsibility for these critically ill patients can help accomplish this goal.

ACKNOWLEDGMENT: The authors thank the nurses in the ED and ICU at Cooper University Hospital for their dedication in implementing state-of-the-art care for our critically ill patients with sepsis.

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