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Stroke volume guided resuscitation in severe sepsis and septic shock improves outcomes

Heath E. Latham [a,*], Charles D. Bengtson [a], Lewis Satterwhite [a], Mindy Stites [b], Dipti P. Subramaniam [c], G. John Chen [c], Steven Q. Simpson [a]

[a] Division of Pulmonary and Critical Care Medicine, The University of Kansas Medical Center, 3901 Rainbow Blvd, MS 3007, Kansas City, KS 66160, United States
[b] Department of Nursing, The University of Kansas Medical Center, 3901 Rainbow Blvd, MS 2018, Kansas City, KS 66160, United States
[c] Department of Internal Medicine, Division of Health Services Research, The University of Kansas Medical Center, 3901 Rainbow Blvd, MS 1037, Kansas City, KS 66160, United States

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ABSTRACT

To determine whether stroke volume (SV) guided fluid resuscitation in patients with severe sepsis and septic shock alters Intensive Care Unit (ICU) fluid balance and secondary outcomes, this retrospective cohort study evaluated consecutive patients admitted to an ICU with the primary diagnosis of severe sepsis or septic shock. Cohorts were based on fluid resuscitation guided by changes in SV or by usual care (UC). The SV group comprised 100 patients, with 91 patients in the UC group. Net fluid balance for the ICU stay was lower in the SV group (1.77 L) than in the UC group (5.36 L) ($p = 0.022$). ICU length of stay was 2.89 days shorter ($p = 0.03$) and duration of vasopressors was 32.8 h less ($p = 0.001$) in the SV group. SV group required less mechanical ventilation (RR, 0.51; $p = 0.0001$). The SV group was less likely to require acute hemodialysis (6.25%) compared with the UC group (19.5%) (RR, 0.32; $p = 0.01$). In multivariable analysis, SV was an independent predictor of lower fluid balance, LOS, time on vasopressors, and not needing mechanical ventilation. This study demonstrated that SV guided fluid resuscitation in patients with severe sepsis and septic shock was associated with reduced fluid balance and improved secondary outcomes.

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1. Introduction

Severe sepsis and septic shock are characterized by peripheral vasodilation associated with excessive release of inflammatory mediators resulting in a decrease in systemic vascular resistance, decreased effective intravascular volume, and resultant tissue hypoperfusion [1]. Early recognition, antibiotic initiation, and fluid resuscitation are integral components of care for patients with severe sepsis and septic shock; current Surviving Sepsis Guidelines recommend a fluid challenge of at least 30 mL/kg of crystalloid as part of initial resuscitative efforts and state that further fluid could be administered based upon improvement in dynamic or static values [2-5].

Multiple systematic reviews have shown that nearly half of patients who were administered a fluid bolus in an ICU setting did not have a corresponding increase in stroke volume (SV) or cardiac output (CO) calling into question the utility of non-targeted fluid resuscitation in severe sepsis and septic shock [6,7]. In addition, a retrospective analysis of the Vasopressin in Septic Shock Trial and other studies of severe sepsis and septic shock patients demonstrated that an increased positive fluid balance is associated with increased morbidity and with mortality [8-10]. In recent years, a number of hemodynamic monitoring devices and techniques were validated to predict fluid responsiveness, including pulse pressure variability, pulse contour analysis, and Doppler derived techniques, each with its own benefits and flaws [11].

Bioreactance is a method that non-invasively measures hemodynamic values, including SV and CO; it achieves these measurements by detecting phase shifts in a small electrical current passed between electrodes attached to the thorax [12]. It is comparable to other hemodynamic measurement tools in assessing SV and CO, but it does not require invasive monitoring [13,14]. Additionally, it is not affected by arrhythmias or type of ventilation (positive or negative pressure). We performed this retrospective analysis to evaluate the hypothesis that a targeted volume resuscitation strategy that aimed to optimize stroke

Abbreviations: CO, cardiac output; CVP, central venous pressure; NICOM, non-invasive cardiac output monitor; SAPS, Simplified Acute Physiology Score; ScvO2, central venous oxygen saturation; SV, stroke volume; SVI, Stroke Volume Index.

* Corresponding author.
E-mail addresses: hlatham@kumc.edu (H.E. Latham), cbengtson@kumc.edu (C.D. Bengtson), lsatterwhite@kumc.edu (L. Satterwhite), mstites@kumc.edu (M. Stites), dsubramaniam2@kumc.edu (D.P. Subramaniam), gchen2@kumc.edu (G.J. Chen), ssimpson3@kumc.edu (S.Q. Simpson).

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volume via non-invasive bioreactance monitoring would result in a decreased fluid balance and improved secondary outcomes in ICU patients with severe sepsis and septic shock.

2. Materials and methods

After obtaining approval from the University of Kansas Institutional Review Board (00001653), we conducted a retrospective chart review and cohort analysis of patients with a diagnosis of severe sepsis or septic shock treated in the medical or transplant ICUs at the University of Kansas Hospital (Kansas City, KS) from April 1, 2014 to September 1, 2014. Consecutive patients admitted to the medical or transplant ICUs were selected based on primary admission diagnosis codes for severe sepsis and septic shock. The time interval for data collection was selected for evaluation because the non-invasive cardiac output monitoring (NICOM) device was available for use in our ICUs starting in April of 2014. The stroke volume guided group of the study comprised patients with the primary admitting diagnosis of severe sepsis or septic shock, as defined by the Surviving Sepsis Campaign International Guidelines 2012, who underwent stroke volume targeted fluid resuscitation guided by NICOM (Cheetah-Medical, Newton Center, MA), during the initial 4 h of their ICU course [2]. For comparison, we chose a similar group of matched consecutive patients with the primary admitting diagnosis of severe sepsis or septic shock, as defined by the Surviving Sepsis Campaign International Guidelines 2012, treated in the same ICU during the same time period, but who had fluid resuscitation guided by usual care at the discretion of the provider. No cases of severe sepsis or septic shock were excluded from analysis during the period of study, and vasopressor use was not required to be included in the study. At the time of the study period and prior to implementing NICOM in our ICU, fluid resuscitation in the usual care group was primarily guided by serial lactates, and bedside clinical assessment [15]. During the study period, fourteen separate Pulmonary and Critical Care faculty rotated, on average, one week per month in the involved ICUs. Fluid management strategy was selected by individual attending or house staff physicians.

All data were abstracted through the Epic (Verona, WI) electronic medical record (EMR) and were collected and managed using REDCap electronic data capture tools hosted at the University of Kansas Medical Center [16]. Demographics and associated conditions were based on data prior to ICU admission. Patient acuity was calculated using Simplified Acute Physiology Score (SAPS) II and was based upon the worst physiologic values in the 24 h surrounding their ICU admission. Net fluid balance was calculated using nurse documented hourly intake and output flowsheets; insensible losses were not calculated. The documentation of intake and output previous to admission to the ICU was inconsistent throughout the data set; and therefore, the decision was made to only collect fluid balance data during the ICU admission, as this documentation was very consistent throughout the data set.

At the time of NICOM implementation, our institution established a standardized procedure for patients receiving SV-targeted fluid resuscitation, involving either a passive leg raise or a 500 mL crystalloid bolus. The procedure, once instituted, calls for patients with evidence of an SVI increase of ≥10% to receive repeated fluid boluses, until there is no further increase in SVI. For those patients undergoing SV-targeted fluid resuscitation, the NICOM device was used within 4 h of admission to the ICU, and the above procedure was followed. Baseline lactate, $ScvO_2$ and CVP measurements were obtained, when available, and in the SV group, post-volume challenge measurements were also recorded. Duration of vasopressor use was calculated to the nearest hour, and number of vasopressors used was determined, regardless of duration of use. Mechanical ventilation and dialysis utilization was determined by any use of those devices in a calendar day.

The univariate analyses were compared using Graphpad® PRISM 6 software (La Jolla, CA). Demographics were compared using descriptive statistics. The continuous variables of SAPS II, fluid balance (4 h, 24 h, 48 h, and ICU Length of Stay (LOS)), ICU LOS, time on vasopressors, and duration of mechanical ventilation were compared using an unpaired *t*-test. Categorical variables including in-hospital mortality, requirement for mechanical ventilation, and requirement for dialysis were compared using Fisher's exact test.

Multivariate analyses with linear and logistic regression were used to determine predictive factors for the following eleven patient outcomes (dependent variables): fluid balance (4 h, 24 h, 48 h, and ICU LOS), hospital mortality, ICU LOS, need for mechanical ventilation and duration, need for vasopressor and duration, and need for acute hemodialysis. The independent variables analyzed in each model were: use of stroke volume guided resuscitation, age, gender, race, SAPS II score, initial MAP, and presence of individual co-morbidities (pulmonary, cardiovascular, neurological, gastrointestinal, renal, and diabetes). The multivariable analyses were computed using IBM SPSS Statistics for Windows, Version 23.0 (Microsoft Corp. Redmond, WA). A two-tailed p-value < 0.05 denoted statistical significance for all univariate comparisons and for predictor variables in the multivariate models.

Table 1
Comparison between SV and usual care groups.

	SV-guided (%)	Usual care	p-Value
Demographics			
Patient no.	100	91	
Age, y	60	59	0.61
Gender (M/F)	49/51	45/45	1.00
SAPS II score	49.64 ± 1.60	49.25 ± 1.69	0.87
Admit SVI pre-challenge (on vasopressors)	39		
Admit SVI post-challenge (on vasopressors)	45		
Admit SVI pre-challenge (no vasopressors)	37		
Admit SVI post-challenge (no vasopressors)	44		
≥10% SVI increase (all patients)	53/100 (53)		
Lactate pre-challenge	3.01		
Lactate post-challenge	2.81		
Admit pulse	96	102	0.12
Admit BP	96/53	112/65	0.0001
Admit MAP	65	78	0.0001
Admit creatinine[a]	1.6	2.1	0.057
Admit lactate	2.82	3.25	0.27
Ethnicity			
White	74 (74)	63 (68)	
Black	14 (14)	19 (22)	
Hispanic	6 (6)	5 (6)	
Asian	3 (3)	1 (1)	
Other	3 (3)	3 (3)	
Co-morbidities			
Pulmonary	18	24	0.22
Cardiovascular	27	28	0.63
Neurological	15	21	0.20
GI	28	33	0.28
Renal	7	9	0.60
Diabetes	24	25	0.62
Source of sepsis			
Pulmonary	39	46	0.11
Abdominal	27	23	0.87
Urological	27	21	0.62
Skin & soft tissue	8	13	0.17
Bacteremia	11	5	0.20
CNS	2	1	0.99
Endocarditis	0	3	0.12
>1 source identified	11	20	0.05

SAPS II = Simplified Acute Physiology Score II, SVI = Stroke Volume Index, MAP = Mean Arterial Pressure, GI = Gastrointestinal.
[a] Creatinine of patients not receiving chronic hemodialysis at time of admission to ICU.

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