The Use of Impedance Cardiography in Predicting Mortality in Emergency Department Patients With Severe Sepsis and Septic Shock

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Abstract

Objectives: Pulmonary artery catheterization poses significant risks and requires specialized training. Technological advances allow for more readily available, noninvasive clinical measurements of hemodynamics. Few studies exist that assess the efficacy of noninvasive hemodynamic monitoring in sepsis patients. The authors hypothesized that cardiac index, as measured noninvasively by impedance cardiography (ICG) in emergency department (ED) patients undergoing early goal-directed therapy (EGDT) for sepsis, would be associated with in-hospital mortality.

Methods: This was a prospective observational cohort study of patients age over 18 years meeting criteria for EGDT (lactate > 4 or systolic blood pressure < 90 after 2 L of normal saline). Initial measurements of cardiac index were obtained by ICG. Patients were followed throughout their hospital course until discharge or in-hospital death. Cardiac index measures in survivors and nonsurvivors are presented as means and 95% confidence intervals (CI). Diagnostic performance of ICG in predicting mortality was tested by receiver operating characteristic (ROC) curve and areas under the ROC curves (AUC) were compared using Wilcoxon test.

Results: Fifty-six patients were enrolled; one was excluded due to an inability to complete data acquisition. The mean cardiac index in nonsurvivors (2.3 L/min·m², 95% CI = 1.6 to 3.0) was less than that for survivors (3.2, 95% CI = 2.9 to 3.5) with mean difference of 0.9 (95% CI = 0.12 to 1.71). The AUC for ICG in predicting mortality was 0.71 (95% CI = 0.58 to 0.88; p = 0.004). A cardiac index of < 2 L/min·m² had a sensitivity of 43% (95% CI = 18% to 71%), specificity of 93% (95% CI = 80% to 95%), positive likelihood ratio of 5.9, and negative likelihood ratio of 0.6 for predicting in-hospital mortality.

Conclusions: Early, noninvasive measurement of the cardiac index in critically ill severe sepsis and septic shock patients can be performed in the ED for those who meet criteria for EGDT. There appears to be an association between an initial lower cardiac index as measured noninvasively and in-hospital mortality.

Keywords: impedance cardiography, severe sepsis, septic shock, early goal-directed therapy

Sepsis is one of the top 10 causes of death nationally, with over 400,000 annual cases of severe sepsis in the United States. The hospital mortality rate for all-cause sepsis is 17.9%. Traditional parameters of assessing the adequacy of resuscitation are limited, and physicians poorly predict ongoing hypoperfusion in critically ill patients. Measurement of hemodynamics is traditionally limited to pulmonary artery catheterization in the intensive care unit (ICU). Research and expert consensus...
recognize the potential of early hemodynamic monitoring, but also question the routine use of pulmonary artery catheters in shock. Impedance cardiography (ICG) offers the potential for safe, noninvasive hemodynamic monitoring that can be easily applied early in resuscitation. The value of this technology in emergency department (ED) patients with severe sepsis or septic shock is ill-defined.

Application of the findings of earlier studies of hemodynamics in septic shock to ED patients is limited because these studies utilized pulmonary artery catheters, took place in the ICU, and had narrow inclusion criteria (fever, hypotension, and subsequent positive blood cultures were all required). The current practice of identifying critically ill patients who benefit most from early, aggressive goal-directed therapy (EGDT) relies mostly on clinical characteristics. We hypothesized that an association exists between the cardiac index measured noninvasively in ED patients undergoing EGDT for severe sepsis or septic shock and in-hospital mortality.

METHODS

Study Design
This was a prospective, observational convenience trial of patients presenting to the ED with severe sepsis or septic shock. Enrolled patients became part of a cohort that was followed until hospital discharge or in-hospital death. The institutional review board approved this study. Written informed consent was obtained from the patient or designated surrogate before data collection began.

Study Setting and Population
The study setting was an urban academic Level 1 trauma center with an annual census greater than 100,000 patients. Patients were enrolled by one of three trained research associates under the supervision of a full-time certified clinical research professional. Research assistants were present in the ED (18 hours/day, 7 days/week) throughout enrollment and data collection.

We screened patients (age ≥18 years) presenting to the ED with signs and symptoms of severe sepsis or septic shock. Patients who met criteria for EGDT (systolic blood pressure [sBP] < 90 mm Hg, mean arterial pressure < 65 mm Hg after 2 L of fluid resuscitation, or initial lactate > 4 mmol/dL) were enrolled only if a central line was placed that measures central venous oxygen saturation (ScVO2).

Patients were excluded if they were pregnant, incarcerated, had environmentally induced hypothermia (<95°F) or hyperthermia (>104°F), if there were burns or tissue damage present on the neck or thorax that precluded monitoring, or if there was any suspicion of coexisting traumatic, cardiogenic, or neurogenic shock.

Study Protocol
We collected necessary information using a standardized case report form. Proper placement and function of the central venous oximetry catheter was confirmed by trained nursing staff. Patients then had the ICG device placed (BioZ, Sonosite, Inc., Bothell, WA) on opposing sides of the neck and thorax in the coronal plane (Figure 1). Each of the four locations of monitoring had two connected leads. Leads at the neck were placed with inferior leads located at the base of the neck. Leads on the thorax were placed with the superior leads at the level of the xiphoid process. Upon confirmation of adequate electrocardiographic monitoring and impedance signals, we obtained pertinent hemodynamic patient information simultaneously with the initial central venous pressure (CVP) and ScVO2.

Clinicians were blinded to all ICG measures. Data were entered into a standard Excel database (Microsoft Corp., Redmond, CA). Mortality was defined as in-hospital mortality.

Data Analysis
Inferential statistics were used to compare demographic, clinical, and hemodynamic features of study patients. Data are presented as means, and 95% confidence intervals (CI) were calculated for mean differences. Data were transformed using log and square root transformations when samples deviated from normality using a modified Shapiro-Wilk test. Statistical comparisons between groups were performed using the Student’s t-test. The area under the receiver operating characteristic (ROC) curve (AUC) was calculated for the primary endpoint of in-hospital mortality using the Wilcoxon method. Prior studies demonstrated a 15% to 30% reduction in cardiac output in nonsurvivors versus survivors. Our historical hospital mortality rate in this patient population was 25%; thus we estimated a necessary sample size of 56 to have a power of 80% (α = 0.05, two-tailed) to detect a 30% difference between the mean cardiac indices of survivors and nonsurvivors.

RESULTS

From August 8, 2007, to May 6, 2009, we screened 135 patients. Seventy-nine were excluded secondary to inability to consent, and one was excluded after enrollment because patient care activities made data acquisition unfeasible; this left a 55-patient cohort. The overall mortality rate was 25.9% (95% CI = 13.6% to 36.4%). Table 1 demonstrates the demographic, clinical, and he-
modynamic characteristics of all patients, survivors, and nonsurvivors.

The mean cardiac index in nonsurvivors (2.3 L/min-m², 95% CI = 1.6 to 3.0) was less than that of survivors (3.2 L/min-m², 95% CI = 2.9 to 3.5), with a mean difference of 0.9 (95% CI = 0.12 to 1.71). The AUC for cardiac index was 0.71 (95% CI = 0.58 to 0.88, p = 0.004). Nine (16.7%, 95% CI = 6.6% to 26.1%) patients had an absolute low cardiac index (<2 L/min-m²). A cardiac index less than 2 L/min-m² was 43% (95% CI = 18% to 71%) sensitive and 93% (95% CI = 80% to 95%) specific for predicting in-hospital mortality.

**DISCUSSION**

Patients with signs and symptoms of severe sepsis and septic shock present a clinical challenge and require early and aggressive resuscitation. Measurement of changes in the cardiac index in response to fluid resuscitation remains the criterion standard for predicting in-hospital mortality. The role that awareness and use of cardiac index may play in the clinical management of critically ill patients is ill defined. CVP is the first and earliest targeted resuscitation measure of EGDT protocols, but it is a static measure with a poor correlation (r = 0.18) to fluid responsiveness and preload dependence. Reviews have demonstrated that changes in stroke volume, cardiac output, or cardiac index are better measures of fluid responsiveness. As an initial step, we have demonstrated that noninvasive assessment of the cardiac index is feasible in this ED subset of patients and that an association exists between the cardiac index on initiation of EGDT and in-hospital mortality. The lower cardiac index and stroke volume in nonsurvivors may be indicative of underresuscitation, hypovolemia, or sepsis-induced myocardial dysfunction and may

| Table 1 Clinical, Laboratory, and Hemodynamic Characteristics of the Study Population |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                | All Patients                     | Survivors                       | Nonsurvivors                   |
|                                | Mean or n (%) | 95% CI              | Mean or n (%) | 95% CI              | Mean or n (%) | 95% CI              |
| Age†                          | 68.6 (47) 63–73.6               | 65.3 (46) 59.1–70.9           | 77.3 (64) 65.6–86            |
| Female sex                    | 26 (47) 33–60                  | 19 (46) 33–59               | 7 (50) 37–63               |
| White race                    | 49 (91) 83–99                  | 34 (83) 73–93              | 13 (92) 85–99             |
| Hx CAD                        | 21 (39) 26–52                  | 12 (30) 18–42               | 9 (64) 51–77              |
| CAD risk factors*             | 1.6 (1.4–1.9)                 | 1.6 (1.4–2.4)               | 1.6 (1.4–2.8)              |
| IVFₒ (Liters)*               | 1.85 (1.4–2.5)                | 2 (1.4–2.8)                | 1.47 (1.4–2.8)             |
| APACHE*                       | 17 (15–19.3)                  | 16.5 (13.8–18.9)            | 18.6 (14.4–25.1)           |
| MEDS                          | 9.9 (8.7–11)                  | 9.4 (8.1–10.8)              | 11.2 (8.8–13.6)            |
| CVP                           | 10.3 (8.9–11.7)               | 10.3 (8.5–12.1)             | 10.0 (7.7–12.3)            |
| Lactate (mg/dL)*             | 3.7 (3.1–4.4)                 | 3.3 (2.7–4.1)               | 4.8 (3.4–6.9)              |
| sBPₒ (mm Hg)                 | 106 (97–115)                  | 107 (98–117)                | 104 (87–125)               |
| HR (beats/min)                | 76 (70–84)                    | 80 (72–89)                  | 67 (56–82)                 |
| Cardiac index                 | 2.96 (2.67–3.26)              | 3.2 (2.89–3.5)              | 2.28 (1.59–2.97)           |
| SV (mL)                      | 57 (50–65)                    | 64 (55–72)                  | 42 (27–57)                 |
| SVRI*                        | 1,640 (1,438–1,871)           | 1,541 (1,361–1,746)         | 1,992 (1,370–2,896)        |

**APACHE =** Acute Physiology and Chronic Health Evaluation score; CAD = coronary artery disease; CVP = central venous pressure; HR = heart rate; Hx = history; IVFₒ = intravenous fluids administered prior to first measurement; MEDS = Mortality in Emergency Department Sepsis score; sBPₒ = initial systolic blood pressure; SV = stroke volume; SVRI = systemic vascular resistance index.

*Log-transformed data.
†Square root-transformed data.
suggest a previously unrecognized need for more aggressive resuscitation. Further study, particularly including more patients and focusing on the response of the cardiac index to resuscitation over time, may clarify this observed association further and improve the early fluid resuscitation of ED patients with severe sepsis.

LIMITATIONS

A selection bias toward excluding sicker patients may be present because patients or a designated surrogate had to provide written informed consent, and no measurements were taken until a central venous oximetry catheter was placed. However, our study mortality was equivalent to institutional experience, suggesting that these limitations may have had little effect. It is conceivable that technical knowledge of the ICG device may limit one’s accuracy, but the monitor easily identifies adequate signal quality, and there is excellent intrarater reliability in personnel with minimal experience.

CONCLUSIONS

Early, noninvasive measurement of the cardiac index in critically ill severe sepsis and septic shock patients can be performed in the ED in those who meet criteria for early goal-directed therapy. There appears to be an association between an initial lower cardiac index as measured this way and in-hospital mortality.

References