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Cardiac output and systemic vascular resistance: Clinical assessment compared with a noninvasive objective measurement in children with shock☆,☆☆

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ABSTRACT

Purpose: To evaluate physician assessment of cardiac output and systemic vascular resistance in patients with shock compared with an ultrasonic cardiac output monitor (USCOM). To explore potential changes in therapy decisions if USCOM data were available using physician intervention answers.
Study design: Double-blinded, prospective, observational study in a tertiary hospital pediatric intensive care unit. Forty children (<18 years) admitted with shock, requiring ongoing volume resuscitation or inotropic support. Two to 3 physicians clinically assessed cardiac output and systemic vascular resistance, categorizing them as high, normal, or low. An investigator simultaneously measured cardiac index (CI) and systemic vascular resistance index (SVRI) with USCOM categorized as high, normal, or low.
Results: Overall agreement between physician and USCOM for CI (48.5% [$\kappa = 0.18$]) and SVRI (45.9% [$\kappa = 0.16$]) was poor. Interobserver agreement was also poor for CI (58.7% [$\kappa = 0.33$]) and SVRI (52.3% [$\kappa = 0.28$]). Comparing theoretical physician interventions to "acceptable" or "unacceptable" clinical interventions, based on USCOM measurement, 56 (21%) physician interventions were found to be "unacceptable."
Conclusions: There is poor agreement between physician-assessed CI and SVRI and USCOM, with significant interobserver variability among physicians. Objective measurement of CI and SVRI may reduce variability and improve diagnostic accuracy.

1. Introduction

Septic shock remains as a major cause of morbidity and mortality in children [1,2]. Early aggressive therapy in children with sepsis or septic shock is crucial for management [3]. Yet, as the pediatric sepsis guidelines specify, it is important to differentiate cold shock (low cardiac output [CO] and high systemic vascular resistance [SVR]) from warm shock (high CO and low SVR), as the treatment algorithms and outcomes may differ [4,5]. Pediatric intensivists tend to rely on physical examination, vital signs, central venous pressure monitoring, markers of perfusion, and laboratory values to clinically assess cardiac index (CI) and systemic vascular resistance index (SVRI), and differentiate cold from warm shock. Studies in hemodynamically compromised adults have shown that physicians are inaccurate in their clinical assessments of CI and SVRI [6-9].

There are little data in children evaluating how well pediatric critical care practitioners differentiate cold from warm shock, likely because the most widely validated method to measure CI and SVRI directly (ie, thermodilution using a pulmonary artery catheter [PAC]) is invasive and infrequently used. There are some data in children showing clinician assessment of CI and SVRI is inaccurate against less well validated but still invasive femoral artery thermodilution techniques [10,11].

Recent advances in noninvasive techniques to measure CI and SVRI in children afford the possibility to study this question more directly. We recently validated that the ultrasonic cardiac output monitor (USCOM) is accurate against thermodilution using a PAC in children [12], further supporting some previous findings [13,14]. In this study, we sought to determine the accuracy and interobserver variability of pediatric physician's assessment of CI and SVRI against (USCOM) in children with septic shock. We hypothesized that physicians are inaccurate in their hemodynamic

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assessments in children with septic shock, and that there is high clinician interobserver variability in these assessments.

2. Materials and methods

2.1. Patients

We performed a single-center, prospective, double-blinded observational study at a tertiary pediatric intensive care unit at Children's Hospital Los Angeles from February 2013 to May 2014. The CHLA Institutional Review Board approved this study (CCI #12-00218), and informed consent was obtained. We included patients 1 month to 21 years admitted to the pediatric intensive care unit with a diagnosis of the following: sepsis, septic shock, or severe sepsis, as defined by the International Sepsis Consensus Conference [15]. In addition, patients had to have ongoing hemodynamic compromise requiring the following: fluid bolus therapy (colloid or crystalloid) of a minimum of 20 mL/kg within 4 hours of enrollment, or inotropes or vasopressors (minimum dopamine $\geq 5\ \mu g\ kg^{-1}\ min^{-1}$ or any therapy with epinephrine, norepinephrine or vasopressin), or systemic vasodilators or phosphodiesterase inhibitors (sodium nitroprusside or milrinone) in the setting of sepsis. Patients with congenital heart disease with intracardiac shunt physiology, valvular heart disease including stenosis or insufficiency, tracheostomy tubes (due to inadequate windows obtained with ultrasound probe), or those unable to cooperate with brief ultrasound measurements were excluded. The exclusion of patients due to cardiac lesions was based on their clinical history and echocardiographic reports (when available).

3. Cardiac index and SVR measurements

Cardiac index and SVR measurements were performed using the USCOM (Sydney, Australia), which is FDA approved and uses continuous-wave Doppler ultrasound technology directed at flow from the aortic or pulmonary valve. The flow from the valve is measured as the velocity-time integral (VTI). A nomogram based on height, weight, and sex supplies aortic or pulmonary valve diameter. The VTI multiplied by valve area gives stroke volume and this multiplied by heart rate gives CO. Entering vital signs and patient data allow for the calculation of hemodynamic variables including CO, CI, SVR, and SVRI.

A single-experienced investigator (AR) performed all USCOM measurements. Physicians were blinded to the measurements by leaving the room when the investigator performed a measurement. Although obtaining the measurement, the screen was set so the investigator saw only the relevant waveform needed to record an accurate signal and the heart rate. Indices such as CO, CI, and SVRI were not displayed on the monitor, so as to limit bias. Three measurements of CI and SVRI were obtained at a given time, and the average value was used for analysis.

For analysis, CI and SVRI were grouped into low, normal, and high, based on the following published standards: CI: low (<3.5 L/min per square meter), normal (3.5-5.5), and high (>5.5); and SVRI: low (<800 dynes•s/cm^5 per square meter), normal (800–1600), and high (>1600) [16,17].

4. Physician assessments

Physicians volunteered to participate for the study. No identifying information of the physician was gathered, except their level of training (resident, fellow, or attending). Two to 3 ICU physicians, ideally of different levels of training, made the clinical assessments of CI and SVRI. For the clinical assessment, the physicians were able to perform a physical examination, review all clinical data available such as, vital signs, urine output, any laboratory information, central venous pressure, and arterial blood pressure. The physicians assessed the patient either immediately before or immediately after a measurement obtained with the USCOM. They were blinded to the USCOM measurement. After examining and reviewing relevant clinical data, the physician completed the physician assessment form, out of sight of the investigator (AR), and described 4 aspects of their assessment: (1) CI (low, normal, high) and SVRI (low, normal, high); (2) listed the clinical signs and information used to come to that conclusion; (3) what, if any, treatment they would implement at this time; and (4) what, if any, treatment to implement if the patient was to develop a new requirement for additional hemodynamic support in the subsequent few minutes.

The completed physician assessment forms were collected in an opaque envelope and analyzed only after completing the 3 USCOM assessments for the individual patient. Serial assessments of the same patient were performed, but required to be separated in time by at least 4 hours, or with a significant clinical change in the patient. The USCOM measurements and clinical assessments were performed within a 5-minute interval of each other and all participating physicians examined the patient within 5 minutes of each other. The investigator was blinded to the clinical assessment as was the physician blinded to the USCOM measurement. In addition, the physicians assessing the patient were blinded to each other's clinical assessment.

All therapy decisions were per the management of the primary care team. The vasoactive medications used included combinations of dopamine and epinephrine, norepinephrine, milrinone, or nitroprusside as determined by the clinical team. The USCOM results were not shared with the clinical team during or after the course of the study.

4.1. Outcome measures and analysis

The primary analysis in this study was the concordance of physician assessment of a patient's CI and SVRI, with measured values from USCOM. Secondary analyses included the interobserver variability in the clinical assessment of CI and SVRI, as well as determination of how level of training affects concordance of clinical assessments and USCOM measurements. Finally, we explored whether there would be potential changes in therapy decisions if USCOM data were available by comparing “acceptable” clinical interventions, based on the hemodynamic state of the patient, to the physicians' answers to the questions regarding interventions. This was intended as exploratory information only, to help understand whether inaccuracies in clinical assessment could have the potential to affect the correctness of therapy decisions. Each combination of CI and SVRI was assigned an “acceptable” clinical intervention as described in Table 1, based on consensus agreement of the 5 authors of the study. The physician's answers were then compared with the “acceptable” intervention table, which was based on USCOM combinations of CI and SVRI. For example, if the clinician recommended an intervention of increasing dopamine based on their clinical assessment, but the USCOM-based hemodynamic state of the patient was high SVR and high CI then the intervention would be deemed “unacceptable.” If the clinician had recommended weaning inotropes or adding vasodilator in the same situation, then the intervention would have been deemed “acceptable” (Table 1).

κ Statistics were used to assess agreement between measurements obtained using the USCOM compared with clinical assessment of CI and SVRI, as well as interobserver variability within physicians, independent of USCOM. We deemed a κ level between 0.6 and 0.8 as demonstration that clinicians were reliable in their assessments of CI and SVRI against an objective tool. Given the different levels of training between the physicians, we expected that there would be at least fair agreement ($\kappa = 0.2$-0.4) between the physicians and the USCOM measurement. We powered the study based upon an expected κ of 0.4, and a desired κ of more than 0.6 to deem the agreement between clinical rating and USCOM acceptable. With these assumptions, the required sample size was estimated at 40 patients, with 238 physician assessments.

5. Results

Forty-three patients were enrolled; 2 patients were excluded due to incomplete consent, and 1 due to early resolution of shock, leaving 40