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Extended Abstract
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Heart Congress 2019: Integral Role of Transthoracic Echocardiography and Clinical Predictors of Mortality in Septic Shock Patients- Issues with Management- Karthik Ananthasubramaniam- Henry Ford Hospital Heart & Vascular Institute, USA

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Introduction

Sepsis is a complex clinical syndrome caused by a dysregulated host inflammatory response to infection, leading to acute lifethreatening organ dysfunction. The inflammatory response results from pathogen-mediated host immune cell stimulation and sequential activation of pro-inflammatory mediators to eradicate invading microorganisms. The exuberant inflammatory response that ensues in sepsis propagates systemic inflammation with resultant end stage damage to the host tissue. Septic shock is the most severe form of sepsis in which profound hemodynamic collapse has ensued despite adequate fluid resuscitation, resulting in substantially increased mortality with reported ranges from 30%-50%. Sepsis is a major cause of admission to the intensive care unit (ICU). It is currently ranked as the 10th leading cause of death in the United States and the leading cause of death in non-coronary ICUs. Sepsis is a major public health concern, accounting for more than $20 billion of the total US hospital costs, and its incidence is increasing given the increased number of aging patients with chronic conditions.

Myocardial dysfunction is a common morbid consequence of severe sepsis and septic shock that has become increasingly more recognized over the past 3 decades. While the exact pathophysiologic mechanisms are not well understood, myocardial depression is thought to be due to circulating inflammatory cytokines and dynamic adaptation of the cardiovascular system. Sepsis-induced cardiac dysfunction is characterized by impairment in contractility, diastolic dysfunction (DD) or both. Existing literature contains a sizable body of work on systolic dysfunction in sepsis; however, less is known about DD and its prognostic implications in critically ill patients with septic shock.

The present study was aimed at identifying the transthoracic echocardiography (TTE) features and clinical parameters that best predict ICU and 90 day mortality in patients with septic shock, with particular attention to the importance of septic shock mediated DD. This study also assessed the role DD severity by grade on outcomes in septic shock. Furthermore, whether DD was worsened or occurred as a consequence of septic shock was investigated.

Materials and Methods

Henry Ford Hospital (Detroit, MI) is a tertiary care center with a large medical ICU comprising 68 beds. We retrospectively reviewed a total of 248 consecutive patients admitted to the ICU with septic shock between January 2011 and April 2013. Patients with septic shock were identified by a computer search of the diagnostic codes-according to the International Classification of Disease, 9th Revision-of all discharge diagnoses. The medical records of all of the patients with a diagnostic code for septic shock were then manually reviewed for verification by investigating physicians. Baseline demographic, clinical and TTE data were obtained at time of ICU admission by reviewing the electronic medical records. Follow-up data was obtained through a review of medical records and the Social Security Death Index. The Institutional Review Board of Henry Ford Hospital approved the study.

Patients were included for analysis in this investigation only if they met criteria for septic shock, defined as known or suspected infection with 2 or more signs of systemic inflammatory response syndrome, organ dysfunction, and hypotension defined as systolic blood pressure less than 90 mm Hg or mean arterial pressure less than 65 mm Hg after a 30 mL/kg fluid bolus or requiring vasopressor therapy. Excluded were patients with suspected cardiogenic shock, acute myocardial ischemia, severe mitral or aortic valve disease, preexisting severe impairment in left ventricular ejection fraction and patients with poor echocardiographic image qualities. Univariate analysis was performed using independent t-tests for continuous variables, and using chi-square tests for categorical variables. Multivariable models were built using clinically relevant variables with $P<0.05$ univariate results, then reduced using manual backwards selection to arrive at a final model identifying independent clinical, systolic and diastolic TTE predictors of mortality during ICU stay and within 90 days of hospitalization. Adjusted odds ratios and 95% CIs were determined.

Discussion

Our study demonstrates that E/e' medial annulus, in conjunction with clinical parameters, may help identify septic shock patients with even higher mortality risk beyond traditional clinical and TTE parameters. The ratio of early transmitral flow velocity (E) to early diastolic septal mitral annulus velocity (E/e') has been shown to be the most

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accurate non-invasive predictor of elevated left ventricular filling pressure. Previous data have confirmed excellent reproducibility in this measurement and have demonstrated an E/e' ratio >15 to be the best Doppler predictor of an elevated (>12 mm Hg) mean left ventricular diastolic pressure. In the present study, an E/e' medial ratio >15 was found to be a significant predictor of short-and long-term mortality in septic shock.

The severity of DD by grade and its association with outcomes in septic shock has not been studied, to the best of our knowledge. In our study, we found that DD severity appears to correlate with increased early and late mortality in septic shock; however, larger sized studies are needed to verify the statistical significance of this observed trend. Another previously unaddressed question was whether sepsis was responsible for transient DD or whether the DD was in fact a pre-existing condition. Our results reveal that there was evidence for DD preceding septic shock; however, there appeared to be a significant progression of DD as evidenced by a higher E/e' as a consequence of septic shock.

Our study also revealed that enlarged IVC diameter determined by TTE, a surrogate for elevated right atrial pressures, was a strong predictor of late mortality. IVC diameter enlargement did not appear to be a reflection of the amount of intravenous fluid resuscitation administered, as the net fluid balance was similar between patients with and without IVC dilatation. However, we found that patients with dilated IVC size did have a higher white blood cell count and lactate level and higher rates of mechanical ventilation suggesting worse signs of septic shock and end organ injury.

Septic shock is the final stage of a disease continuum that begins with infection and progresses to bacteremia, sepsis, severe sepsis and ultimately septic shock. Septic shock is the leading cause of ICU morbidity and mortality. The frequency of hospitalization for severe sepsis doubled between 1993 and 2003 and continues to grow rapidly, with mortality of severe sepsis remaining as high as 40% despite significant advances in treatment. Acute, profound circulatory collapse resulting in multi-organ failure is the hallmark of septic shock. During septic shock, vasodilatory effects of bacterial endotoxin and endogenous vasopressin deficiency alter the systemic vascular resistance resulting in misdistribution of blood flow and inadequate oxygen delivery.

Conclusions

Our study demonstrates that TTE combined with tissue Doppler estimation of filling pressures (E/e') in conjunction with simple and widely available clinical parameters, such as APACHE II score, lactate levels, age, urine output and hematocrit, may help target more aggressive supportive and resuscitative efforts and closer follow-up in patients with septic shock to prevent early and late mortality. Our study reemphasizes the usefulness of E/e' in critically ill patients, negating prior reports of lack of value of this parameter. Concept/design, Data analysis/interpretation, Drafting article, Critical revision of article, Approval of article, Statistics, Funding secured by, Data collection, Other.)

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