

Precision medicine and the federal sepsis initiative!

Paul E. Marik, Joseph Varon

In his State of the Union address before both chambers of the US Congress on 20 January 2015, President Barack Obama announced the launch of a new initiative called Precision Medicine, "I want the country that eliminated polio and mapped the human genome to lead a new era of medicine - one that delivers the right treatment at the right time." At a White House Press briefing on 30 January 2015 President Obama further commented that "Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals." In complete antithesis to this approach, the National Quality Forum (NQF #0500) (1) and the Center for Medicare & Medicaid Services have developed and mandated the "SEP-1 Early Management Bundle for Severe Sepsis and Septic Shock". In the FY 2015 IPPS/LTCH PPS final rule (p. 50236), published on 22 August 2014, the Centers for Medicare & Medicaid Services (CMS) adopted this composite measure for the Hospital Inpatient Quality Reporting Program for discharges occurring on or later than 1 October 2015. According to this rule, all patients admitted to hospitals in the United States who are suspected to have a diagnosis of sepsis require a blood lactate measurement, blood cultures and the administration of broad-spectrum antibiotics within 3 hours of presentation to hospital. (2) Those patients with hypotension or a lactate concentration >4 mmol/l are required to receive a 30 ml/kg bolus of crystalloid within this time period. (2) CMS has officially stated that "there are no exclusions to the 30 ml/kg amount based on comorbidities such as heart failure (HF), end stage renal disease (ESRD) or any other condition." This approach to fluid management ignores basic human physiology and the complex pathophysiologic

changes that occur with sepsis. (3,4) The Mayo Clinic recently reported their experience with the early goal directed therapy (EGDT) resuscitation protocol as advocated by the Surviving Sepsis Campaign. (5) In this study, which included 405 patients with severe sepsis and septic shock, 67% of patients had clinical evidence of fluid overload with fluid overload being an independent predictor of death. It is likely that over 50% of patients treated by the SEP-1 fluid mandate will be harmed by this approach. (3) **Figure 1** illustrates the hemodynamic profile of a patient harmed by the SEP-1 mandate.

Furthermore, according to the SEP-1 bundle, physicians are required to document reassessment of the volume status (after the 30 ml/kg fluid bolus) in all patients with either "a focused examination including vital signs, cardiopulmonary, capillary refill, pulse and skin findings" or measurement of the central venous pressure (CVP), saturation of central venous blood (ScvO₂) or a bedside cardiovascular ultrasound. While the clinical signs listed may be helpful for identifying inadequate perfusion these signs are unable to determine volume status. (6) Furthermore, the CVP is no more accurate in predicting fluid status than flipping a coin. (7) Three large randomized controlled trials have demonstrated that titrating therapy to the ScvO₂ has no clinical benefit. (8-10) In addition, ultrasonography and echocardiography have limited utility for assessing volume status in critically ill patients. (3) These methods of assessing volume status are unsupported by scientific data and likely to lead to further fluid overload.

The sepsis bundle is likely to have other negative consequences, including the risk of inappropriate application of the sepsis bundle to patients without infections resulting in the inappropriate overuse of antibiotics with their attendant adverse effects and the increased use of unnecessary laboratory tests. Clinicians together with hospital informatics specialists will need to develop methods to document the information required for compliance with the SEP-1 bundle. Data abstractors will then need to resolve over 140 discreet data queries on each patient with presumed sepsis to determine compliance with the SEP-1 bundle. This massive reporting requirement will place an enormous administrative burden on hospitals.

From Eastern Virginia Medical School, Norfolk, VA, USA (Paul E. Marik) and University General Hospital, Houston, TX, USA (Joseph Varon).

Address for correspondence:

Paul Marik, MD
Eastern Virginia Medical School
825 Fairfax Av, Suite 410, Norfolk, VA 23507, USA
Email: marikpe@evms.edu

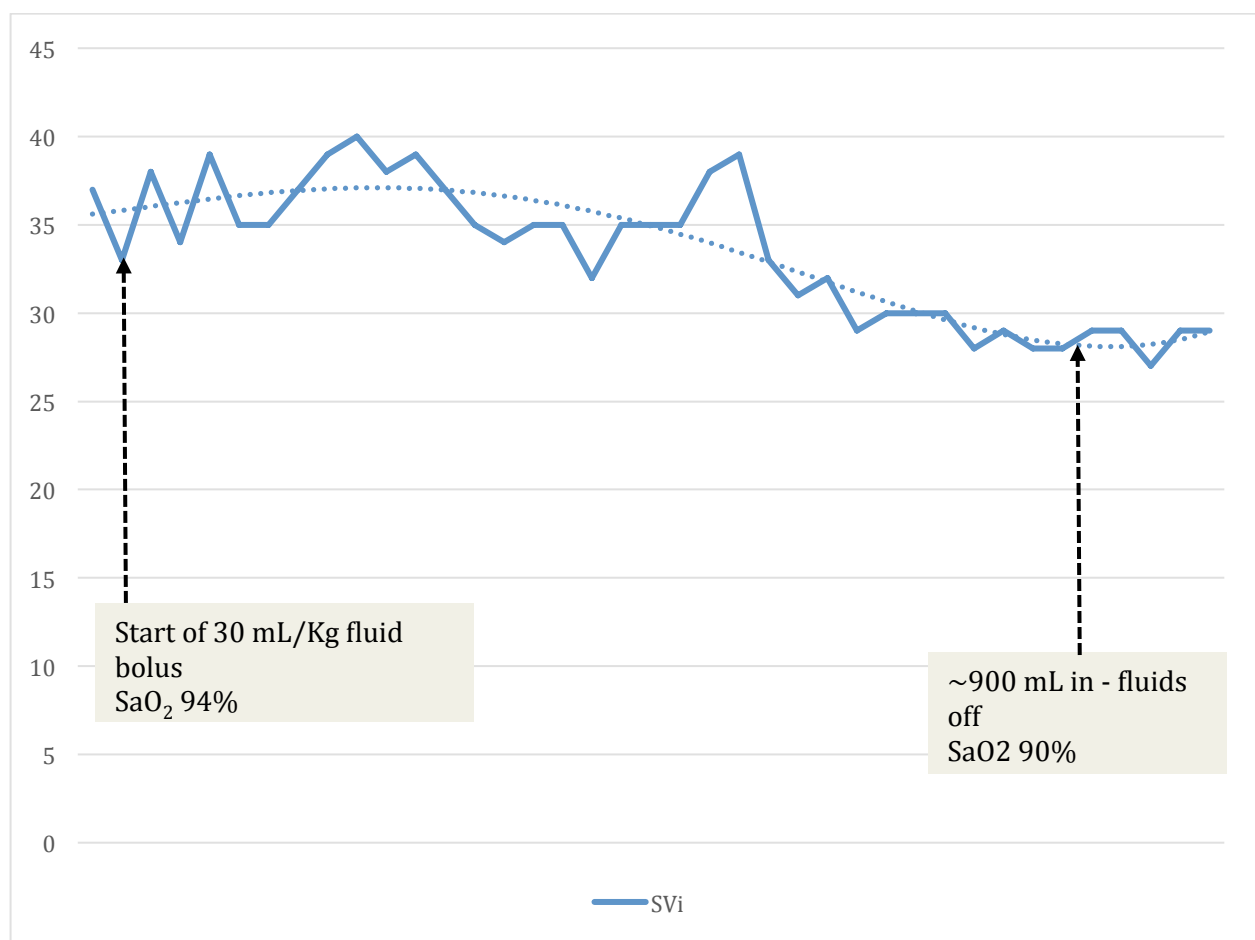
Sepsis is amongst the most complex of diseases known to man. (3,4,11) Each septic patient is unique, with a unique set of genes and unique comorbidities who respond to illness and its treatment in a unique and unpredictable manner. (12) Patients with sepsis need to be managed by precision medicine, that is, a physiologically based, individualized, adaptive and timely treatment approach. Rigid protocols and policies have little

place in the management of these complex patients. The SEP-1 management bundle is not supported by scientific data, is likely to be harmful to many patients and must be abandoned.

Acknowledgment

The author has no real or perceived conflict of interest with regards to the contents of this paper.

Figure 1. 76-year-old normotensive patient with presumed “urosepsis” with a lactic acid concentration of 4.6 mmol/L



Legend: The patient received a fluid bolus of 30 ml/kg on presentation to the Emergency Department as required by the federal regulations. The patient’s stroke volume index (SVi) and arterial oxygen saturation were being monitored continuously. After about 20 minutes the patient’s bedside nurse noted a fall in SVi, a fall in arterial oxygen saturation with the patient complaining of increasing shortness of breath. The fluid bolus was stopped at this point. This patient would fail to meet the SEP-1 quality indicators as she had not received the full 30 ml/kg fluid bolus.

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