The New Treatment Paradigm

Speaker: Paul E Marik, MD.
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Where: 1st floor conference room, IRP II

Abstract:

In 2001 Emanuel Rivers and collaborators published “Early goal-directed therapy in the treatment of severe sepsis and septic shock”, in which they compared two protocols for the early resuscitation of patients with severe sepsis and septic shock. Both protocols used the central venous pressure (CVP) to guide therapy. The “treatment arm” (EGDT) required placement of an oximetric central venous catheter with interventions to maintain the saturation of the central venous oxygen greater than 70%. The >250-patient study reported a 28 day mortality of 49% in the control group and 33% in the EGDT group. The scientific underpinning of the study was flawed, however. EGDT was based on elements that were not supported by evidence-based literature, and the results of the study were “too good to be true”. The basic premise of EGDT was to optimize tissue oxygen transport to reverse tissue hypoxia with the use of continuous monitoring to pre-specified physiological targets. This premise is flawed because bioenergetic failure and cellular hypoxia are likely only pre-terminal events in patients with septic shock. Nevertheless, based on this non-blinded, single-center study, EGDT became regarded as the “standard of care” around the world. It was endorsed by major medical societies and organizations and formed the basis of the 6-hour resuscitation bundle of the 2004, 2008, and 2012 Surviving Sepsis Campaign. Over 30 before-and-after studies were published “claiming” that EGDT reduced mortality. These studies were used to support the notion that EGDT improved the outcome of patients’ with sepsis. However the vast majority of these studies were retrospective, uncontrolled cohort studies where the investigators had vested interests in the outcomes of the studies. In 2014, 13 years after the publication of the EGDT study the ProCESS and ARISE studies were published. PROMISE is the last of the trilogy of large, randomized multicenter studies which demonstrated that EGDT does not improve the outcome of patients with severe sepsis and septic shock. Patients in the EGDT arm of PROMISE had worse organ-failure scores and a longer stay in the ICU with increased use of resources and increased costs. Like most trilogies, it is clear that EGDT was based on “science fiction”. Finally, after aggressively promoting EGDT for over a decade, the Surviving Sepsis Campaign has now abandoned this approach. Like much in critical care, a “less is more” approach appears to apply to the management of patients with sepsis. Early identification, timely use of appropriate antibiotics, a physiological hemodynamically guided approach to fluid management, the early use of norepinephrine, and early source control appears to be a prudent approach to the management of patients with severe sepsis and septic shock.

Biosketch:

Dr Marik received his medical degree from the University of the Witwatersrand, Johannesburg, South Africa. He was an ICU attending at Baragwanath Hospital, in Soweto, South Africa. During this time he obtained a Master of Medicine Degree, Bachelor of Science Degree in Pharmacology, Diploma in Anesthesia as well as a Diploma in Tropical Medicine and Hygiene. Dr Marik did a Critical Care Fellowship in London, Ontario, Canada, during which time he was admitted as a Fellow to the Royal College of Physicians and Surgeon of Canada. Dr Marik has worked in various teaching hospitals in the US since 1992. He is board certified in Internal Medicine, Critical Care Medicine, Neurocritical Care and Nutrition Science. Dr Marik is currently Professor of Medicine and Chief of Pulmonary and Critical Care Medicine, Eastern Virginia Medical School in Norfolk, Virginia. Dr Marik has written over 400 peer reviewed journal articles, 50 book chapters and authored four critical care books..