



# Is it time to implement door-to-needle time for “infection attacks”?

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Despite decades of research investigation, efforts to increase awareness and quality improvement initiatives efforts, morbidity and mortality due to severe sepsis and septic shock remains unacceptably high [1]. There has been an extensive search for novel adjunctive therapies and treatment strategies not limited to an array of immune-modulatory agents, anti-coagulants, and supportive treatments involving glucose control, fluid therapy, and vasopressor, inotropic, and organ support [2]. While gains in general associated with the outcomes of critical illness have been achieved, improvement in outcomes associated specifically with severe sepsis and septic shock management in recent years has been at best modest.

Antibiotic therapy has been a central aspect of sepsis and septic shock management in the modern era. A substantial body of observational studies has shown that delay in the time to receipt of antibiotics is associated with adverse outcome among patients with severe sepsis and septic shock [3, 4]. While guidelines recommend that antibiotics be administered within 1 h, it must be recognized that this has not been proven in a randomized trial and that controversy still exists as to what may define a clinically significant delay or threshold for antibiotic initiation [5, 6].

In a recent article in this journal, Bloos et al. report the results of a cluster randomized trial within 40 German ICUs comparing a multi-faceted enhanced educational and feedback program with a control group receiving standard education surrounding antibiotic therapy of sepsis and septic shock for the primary outcome of 28-day mortality [7]. The multi-faceted intervention resulted in neither a significant reduction in mortality

nor a reduced time to receipt of antimicrobial therapy. However, the overall finding was that each 1-h delay in antibiotic therapy or source control was associated with a 2 or 1% increase in mortality, respectively.

While not demonstrating that the study intervention reduces time to antibiotic therapy (and thus in turn mortality), this study does provide further evidence to add to the evolving body of literature supporting the importance of early antibiotic therapy on improved sepsis outcome. Indeed, to definitively prove that early therapy improves outcome, the best experimental method would be to randomize patients to early compared to late therapy. Obviously, ethical considerations would preclude such a study. Bloos et al. are praised for their efforts to attempt to address this question though an indirect, but ethically appropriate, design. Although not conclusively proven, as a result of the large and increasing body of observational evidence, clinical plausibility, and feasibility, the recommendation for early therapy in sepsis and septic shock in our opinion remains prudent [1].

A second major consideration of this study surrounds why the intervention did not have a significant effect. The median time to treatment was 1.5 h in the intervention group and this was not significantly better than the control group [7]. It is important to note that the control group did receive educational components of biannual lectures and newsletter updates. Thus, it may not necessarily be that the intervention had no effect but rather the added components of the intervention were not significantly better than a basic intervention among the controls. Indeed, sepsis and septic shock management has received extensive attention and is the subject of quality improvement initiatives at local, regional and international venues. The possibility therefore exists that the benefit to further awareness and education is not the issue at hand, and delays may be related to other factors,

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for example practical aspects related to the preparation of medications in the pharmacy.

It is noteworthy that, even with the multifaceted intervention, one-quarter of the patients did not receive treatment for 5 h or longer, indicating that significant room exists for improvement in the process.

We believe that this study represents a major and important work. While it does not definitively prove the case, it does provide further evidence to support the practice of early therapy and source control in patients with severe sepsis and septic shock. However, this study leaves us with the question as to how we may further improve antibiotic management practices in severe sepsis and septic shock. Fundamentally, administration of antibiotics is not a complicated process and there is no apparent practical reason why high rates (i.e. >95%) rates of early (<1 h) therapy could not be achieved. Looking to other disciplines, we observe that high standards of rapid identification, investigation, and administration of even high-risk thrombolytic therapies to patients with myocardial infarction and stroke can be achieved [8]. The concept of “door-to-needle” has been popularized in these cases as well as the use of colloquial terminology of “heart attacks” or “brain attacks” in public awareness campaigns [9]. Is it now time that the concept of door-to-needle time be applied to “infection attacks”?

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#### Compliance with ethical standards

#### Conflicts of interest

The authors declare that they have no competing interests.

Received: 6 April 2017 Accepted: 7 April 2017

Published online: 2 May 2017

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