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Severe Sepsis: Stay and Play or Scoop and Run?

To the Editor:

As evidenced by common adages such as “the golden hour” in trauma care and “time is meat” for acute coronary syndrome and cerebral ischemia, it is widely recognized that many outcomes are time dependent. Consequently, protocols have been developed for these situations to reduce time loss between the first patient contact and treatment, whether on the scene, during transport, or in the hospital. In sepsis, we are lagging behind. In the December 15 issue of the *Journal*, Seymour and colleagues point to the importance of rapid diagnosis and intervention for sepsis (1). They focus on the opportunities for treatment in the prehospital interval. The success of sepsis bundles highly depends on the correct and early recognition of the patient with severe sepsis or septic shock. Seymour and colleagues postulate that a critical window for diagnosis and treatment may have already passed by the time the patient is admitted to the emergency department (ED). This is important because, in their study, the sepsis patient group was even larger than those with myocardial infarction or stroke. Among the patients not diagnosed with severe sepsis prior to ED admission, fewer received bag-mask ventilation and endotracheal intubation, and a trend was found for less supplemental oxygen and peripheral intravenous access (<30%). Whether this resulted in a higher mortality rate was not shown, however. In our university hospital's ED, 44% of all patients initially presenting with suspected sepsis were later diagnosed with severe sepsis and 6% with septic shock. More than 90% of these patients arrived at the ED with intravenous access and supplemental oxygen. The time from presentation to intravenous antibiotics was 54 minutes for patients with severe sepsis and

45 minutes for patients with septic shock, and the time to fluid infusion according to our sepsis protocol was 15 minutes and 4 minutes, respectively (unpublished data). We think that for both our patients and the patients from Seymour and colleagues' study, a substantial improvement could be achieved in the prehospital setting by further increasing the recognition of septic patients (2), thus resulting in prompt peripheral access, a sooner start of fluid resuscitation, and transfer to the ED as fast as possible. Arriving at the hospital, this treatment should be extended by a dedicated sepsis team to a complete sepsis bundle, including intravenous antibiotics. We should evaluate the timeliness and adequacy of sepsis treatment throughout the whole period from initial ambulance call to ultimate diagnosis in a manner analogous to trauma and ischemic events.

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Reply

From the Authors:

In their response to our article (1), Ligtenberg and colleagues suggest that time-sensitive conditions, such as severe sepsis, may benefit from systems of care similar to trauma or ischemic stroke, and that both future study and implementation of such systems will rely on accurate diagnosis of severe sepsis at the frontier of critical care—during the prehospital phase.

We agree wholeheartedly. Of course, the leveraging of the prehospital period to improve care relies in part on patient identification and stratification, a challenging task given the difficulty in recognizing and diagnosing sepsis. One approach is to integrate a quick history and physical with physiologic or serum biomarkers that can be deployed in prehospital care. Such biomarkers would require adequate evaluation, including assessment of their feasibility and their incremental value over existing approaches.

Ligtenberg and colleagues also suggest a suite of treatments that might be more effectively deployed if commenced in the prehospital setting. We certainly endorse evaluation of such interventions, again with attention to both feasibility and incremental value over current care. We would further add that, in addition to specific prehospital interventions, another key advantage of early identification and stratification is to determine *where* the patient should be taken. Many strategies for optimal early care of severe sepsis and septic shock may be better implemented at select centers of excellence. Yet, such

centers make no sense if there is no mechanism by which to preferentially route patients.

Taken together, the many thousands of avoidable deaths from severe sepsis demand we explore innovative approaches to treatment. Should we solve the riddle of early and rapid diagnosis, many promising interventions at the patient and system level await study during prehospital care.

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Survival Benefits of Liver Transplant in Severe Hepatopulmonary Syndrome

To the Editor:

We read with great interest the excellent review article that included a discussion on hepatopulmonary syndrome (HPS) by Fritz and colleagues (1). The authors specifically comment on the poor post-liver transplant (LT) survival in HPS patients with severe hypoxemia who have a $\text{PaO}_2 < 50$ mm Hg and macroaggregated albumin shunt fraction of $>20\%$ (2). Those early post-transplant outcomes are not mirrored in recent data from Gupta and colleagues (3) and our group (4) that show excellent post-LT survival even in patients with severe HPS. Although patients with severe and very severe HPS (baseline $\text{PaO}_2 < 60$ mm Hg and < 50 mm Hg, respectively) may have prolonged post-LT hypoxemia and increased hospital length of stay, we found no evidence for increased post-LT mortality in these subgroups. Additionally, we did not find a post-LT survival difference between HPS patients ($n = 49$) and a contemporary cohort of 1,816 LT patients without HPS (4). One can speculate that this improved survival (especially in the model for end-stage liver disease exception era after 2002) is related to advances in intensive care unit and hospital protocols for managing end-stage liver disease, critical illness, and hypoxemia (low tidal volume ventilation, sepsis bundles, noninvasive ventilation, etc.)

HPS patients have a very dismal prognosis without LT. Current post-LT survival data strongly challenge the notion of withholding LT in patients with severe hypoxemia (5).

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Pulmonary Vascular Complications Include Varices in the Tracheobronchial Tree

To the Editor:

For the sake of completeness, the account of pulmonary vascular complications of liver disease by Fritz and colleagues (1) also ought to include the occurrence of varices in the tracheobronchial tree (2, 3), the latter in association with esophageal varices attributable to liver cirrhosis. Tracheal varices occurring in this context were documented in a 32-year-old man who presented with hemoptysis against a background of previous documentation of stage 3 hepatic fibrosis and esophageal varices. Contrast material-enhanced computerized tomography of the chest showed extensive collateral vessels in the mediastinum and multiple nodules in the mid and dorsal portion of the trachea. Bronchoscopy revealed submucosal tortuous varices with active bleeding (2). Bronchial varices were reported in a 57-year-old man who presented with hemoptysis and a previous history of cirrhosis complicated by bleeding esophageal varices, the latter requiring repeated endoscopic ligation. On bronchoscopy, large dilated submucosal veins were seen, consistent with bronchial varices (3). In both of these instances (2, 3), especially in the first case (2), the occurrence of tracheobronchial varices appeared to be part of the natural history of liver disease. Bronchial varices have, however, also been reported subsequent to sclerotherapy for esophageal varices (4, 5). In the latter context, it is unclear whether or not bronchial varices were attributable to the latter treatment modality.

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