Discussion

Our findings suggest that new-onset AF during suspected infection meets the Sepsis-3 conceptual criteria of an acute organ (cardiac) dysfunction associated with a high risk of mortality. Among critically ill patients, new-onset AF showed small improvements in prognostic validity as compared with the Sepsis-3 model and potentially identified "sepsis" before Sepsis-3 criteria in a small number of ICU patients. New-onset AF was associated with increased mortality proportionate to an increase in SOFA score of ~4 points.

Our findings have limitations. Our ICU cohort likely underestimated the number of patients who developed new-onset AF before meeting Sepsis-3 sepsis criteria, because our patients likely had higher SOFA scores than a non-ICU population. Similarly, the rate of new-onset AF in our study was lower than previous estimates of rates of new-onset AF in critically ill patients with sepsis (4), likely due to cases of new-onset AF that occurred before ICU admission that were coded as preexisting AF using our algorithm. Thus, our findings likely represent conservative estimates. Further studies should examine how new-onset AF may affect prognostic validity outside the ICU.

Our study highlights strengths of the conceptual model of Sepsis-3, as well as limitations of the SOFA score as an operational sepsis definition. The concept that sepsis may be defined as organ dysfunction related to a dysfunctional response to infection provides a framework for including new information within the Sepsis-3 definition. However, the SOFA score was not intended to provide an account of all organ dysfunction or to provide the best predictive model during sepsis; it was chosen to represent sepsis-associated organ dysfunction for its simplicity and familiarity (1). Similar to new-onset AF, there are possibly other infection-associated, life-threatening manifestations of organ dysfunction that incrementally improve prognostication and thus may be considered as "sepsis-defining organ dysfunction" and included in future concepts of "sepsis." Given plausible mechanisms linking infection to new-onset AF (2, 3) and the high risk of death among patients with new-onset AF and suspected infection, we suggest that future sepsis investigators continue to explore new-onset AF as a potentially sepsis-defining sign of cardiac dysfunction.

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Against Another Nonspecific Marker of Perfusion

To the Editor:

We read with interest the article by Frencken and colleagues and the accompanying editorial by Bonk and Meyer regarding the use of high-sensitivity troponin (hs-Tn) in pneumonia (1, 2). We applaud the authors on their publication of useful manuscripts regarding this emerging topic.

Elevated troponin levels are found in nearly half of critically ill patients, using standard troponin assays (3). Thus, it comes as little surprise that 85% of critically ill patients with pneumonia would have an elevated hs-Tn level. The challenge facing clinicians has to do with how to use these data. The pathophysiology of troponin elevation in this context is multifactorial (e.g., including inflammatory injury to myocytes, as

well as myocardial oxygen supply–demand mismatch). Troponin elevations generally do not reflect acute coronary occlusion or stenosis. Rather, troponin elevation in this context functions largely as a marker of mortality (3).

These articles are important for promoting awareness of the frequency of troponin elevation in critically ill patients. All too often, such elevations are misinterpreted as evidence of coronary artery disease, leading to inappropriate use of anticoagulation and cardiac catheterization. This potential cascade of downstream testing and procedures that may result from the widespread application of hs-Tn suggests that we should exercise restraint in obtaining this test.

One conceivably rational use of troponin in the context of a severely ill patient with pneumonia could be as a disease severity marker to facilitate risk stratification. For example, patients with a troponin above a certain level are at increased risk for death, and therefore might potentially benefit from more intensive care. However, we already have validated risk-stratification tools to determine which patients require more intensive care, such as the American Thoracic Society criteria. Furthermore, Frencken found that hs-Tn was less specific as a mortality indicator compared with standard troponin assays. Thus, it is doubtful that hs-Tn could add independent and useful information beyond available risk-stratification tools.

Bonk and Meyer opined that troponin might be used as a perfusion target for resuscitation, perhaps based on the finding by Frencken and colleagues that a downward trajectory of hs-Tn was associated with lower mortality compared with persistent elevation (1). We caution against this approach for many reasons. The mechanism of elevated troponin in these patients is complex, multifactorial, and not necessarily closely related to perfusion. Furthermore, troponin can be elevated by a diverse range of pathologies (e.g., pulmonary embolism, chronic kidney disease, and heart failure) (4). With an extensive list of possible mechanisms and etiologies that may often coexist, it is unclear how this single laboratory test could specifically assess perfusion. If troponin were related to myocardial oxygen supply–demand mismatch, how would we change our approach from the default (i.e., treating the underlying cause)? And importantly, how many patients might suffer from the iatrogenic effects of additional interventions?

Wide application of hs-Tn to assess perfusion in the critically ill would be, at best, another blunt instrument among many unhelpful tools in guiding patient management. Consider the current state of assessing and treating serum lactate, widely practiced because of Surviving Sepsis Guidelines. Evidence supporting this practice is lacking, with a recent study suggesting that lactate was no more effective at gauging perfusion than capillary refill time (5). Given the current state of evidence, we advocate for targeted use of troponin testing for the evaluation and management of suspected myocardial ischemia based on history, physical exam, point-of-care echocardiography, and electrocardiogram findings only.

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Troponin in Sepsis

To the Editor:

Frencken and colleagues measured high-sensitivity cardiac troponin I (hs-cTnI) levels in patients with community-acquired pneumonia and sepsis, and reported elevations above the upper limit of normal in 85% of their cohort (1). Their interpretation of this result was that myocardial injury due to oxygen supply–demand mismatch was responsible for the elevated hs-cTnI.

The authors' findings are interesting, and the associations between elevated hs-cTnI and abnormalities in laboratory tests related to inflammation and coagulation deserve exploration. Nevertheless, we are troubled by certain aspects of the report.

First, the upper limit of normal for elevated hs-cTnI is based on levels in a reference population of healthy volunteers without apparent disease. To apply that cutoff to patients with severe acute disease may not be appropriate (2). Indeed, recent data suggest that the cutoff for abnormal hs-cTnI in acutely ill hospitalized patients may be over four times higher (3). The results of the current study serve mainly to confirm prior studies showing that elevated troponin is a common finding in patients with sepsis (4).

Second, the claim that elevated hs-cTnI represents myocardial ischemia appears to be largely unsupported. Hs-cTnI is a specific