Sao Paulo, March 29, 2016

Dear partners,

As you might be aware, recently the Society of Critical Care Medicine (SCCM) and the European Society of Critical Care Medicine (ESICM) promoted a new consensus conference and published the new sepsis definitions, known as Sepsis 3.0. There are several positives changes in these new definitions. For the first time, the consensus board tried to base themselves on the available data and not on expert opinion. The criteria for systemic inflammatory response syndrome (SIRS) are no longer required for the diagnosis of sepsis and LASI consider this as an important improvement. Sepsis is now defined as a life-threatening organ dysfunction secondary to a dysregulated host response to infection. We fully agree that the presence of SIRS criteria for sepsis diagnosis is not obligatory. Although SIRS criteria remain of upmost relevance as a screening tool for potentially infected patients, particularly in the context of quality improvement programs, they are not fundamental to define the presence of sepsis. We know that many critically ill patients with sepsis do not develop SIRS criteria. LASI did not change its screening tools, but in our quality improvement program the SIRS criteria is no longer required for inclusion of patients in our database. We also acknowledged as a positive change the nomenclature simplification: no more “severe” sepsis but rather only “sepsis”. Over time, this will be an important shift in order to enhance the association of the word sepsis with a serious condition in terms of promoting better understanding of sepsis by health professionals and lay people. Thus, we also adopted a new nomenclature: infection without dysfunction, sepsis and septic shock. The term "severe sepsis" is no longer available in all LASI tools. However, we did not modify the criteria used to define organ dysfunction for the following reasons.

Although LASI has been invited to read the document and endorse it, we chose to reject our endorsement, along with other highly qualified societies such as the American College of Chest Physicians, the American College of Emergency Physicians and the Canadian Critical Care Society. The Sepsis 3.0 board was constituted only by representatives of developed countries without any representatives of resource-limited countries. This absence of diversity might have compromise the ability to assess the impact of these new definitions in settings different from those of the data that based the changes. Although this limitation is recognized by the authors, we still thought our endorsement was not possible as the consequences would not be different just because of this acknowledgement. The main reasons for our decision are as follows:

1. Organ dysfunction was defined as a change in 2 points in the Sequential Organ Failure Assessment (SOFA) score as a consequence of infection. Septic shock is now defined as the presence of hypotension requiring vasopressors to maintain mean arterial pressure ≥ 65 mmHg associated with lactate ≥ 2 mmol/L, after adequate fluid resuscitation. Thus, hyperlactatemia is a necessary component, if available, for the definition of septic shock. The new concepts limit the criteria for defining the presence of organ dysfunction and will select a more severely ill population. For example, patients with hypotension as a single dysfunction without vasoactive drugs or patients with a Glasgow Coma Scale 13 or 14 do not meet the new criteria for organ dysfunction as they score 1 point in SOFA. Patients with hyperlactataemia, even higher than 4.0 mmol/L, without any other dysfunction would also be considered as having uncomplicated infection as lactate is not included in the SOFA score. The new criteria assume that patients with severe hyperlactatemia but without hypotension have no higher risk of death. We disagree because although the presence of both variables clearly increases the risk of death, both are independent risk factors. The new definitions might lead to a situation in which a patient with platelet counts of 99,000 cels/mm^3 or bilirubin 2.1 mg/dL or pO_2/FiO_2 ratio of 290 will be considered as having sepsis, while a patient with lactate above 4 mmol/L, and no other dysfunctions, will have

only "uncomplicated infection." This may be of interest to the more privileged countries today suffering with excessive sensitivity, but goes against the interests of developing countries, where we are trying to raise awareness.

2. LASI believes that there is not enough scientific evidence to change the definitions for organ dysfunction in the way it was proposed. The choice of 2 points change in the SOFA score as the new criterion was based on a comparison of the predictive ability of this criterion as compared to the presence of two SIRS criteria, which means a better ROC curve for change in SOFA when compared with the ROC of two SIRS criteria. Our understanding is that there is no sense in comparing the ability to predict death between a dysfunction score (SOFA) and inflammatory response criteria (SIRS). Clearly, any score involving dysfunction should have better performance. However, the old severe sepsis definition included not only the presence of SIRS but also at least one organ dysfunction. This comparison was not made by the authors.

2. Our understanding is that the new qSOFA score is a severity score suitable for identifying patients at high risk of death or ICU stay for more than 3 days in the settings where the data came from. In this sense, it has been scientifically validated. However, the authors suggested qSOFA as a screening tool. The statistical model used aimed to predict morbidity and mortality and has not been validated as a patient screening strategy. Therefore, we fully disagree with Figure 2 of the definitions' manuscript, wherein qSOFA is used for screening and management of patients. In our quality improvement programs, our goal is not to identify patients at high risk of death but rather to identify patients at high risk of deterioration. The qSOFA has three criteria, assigning a point for hypotension (SBP ≤100 mmHg), high respiratory rate (≥22 breaths per minute) and decreased level of consciousness. The score ranges from 0 to 3, and the author consider qSOFA positive when there are two or more points. In countries with high mortality and delay in detecting patients awaiting the occurrence of two qSOFA criteria for triggering a sepsis protocol may not be suitable. LASI screening strategies always included the presence of these three variables,

hypotension, dyspnea and mentation. However, we believe that any of them should trigger a medical team to assess the patient for sepsis. Thus, this score would not apply to the reality of many Brazilian institutions as it requires, basically, the presence of two dysfunctions and not just one. These patients already have high mortality in our country. Any quality improvement process in developing countries should focus on the early detection of possible infection including the use of SIRS criteria. In an attempt to evaluate the role of qSOFA in Brazilian hospitals, LASI is now collecting these data in our quality improvement program.

The Surviving Sepsis Campaign recently stated that they will not change the criteria used to define organ dysfunction in their quality improvement program and they will maintain hyperlactatemia as one of them. Thus, the LASI opted for alignment with that decision and to maintain our data collection based on the previous organ dysfunction criteria as well the previous septic shock criteria.

We hope we have contributed to clarify these points and we will continue to collaborate with all of our partners. We are at your disposal to further clarification.

Regards,

LASI Team

References

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