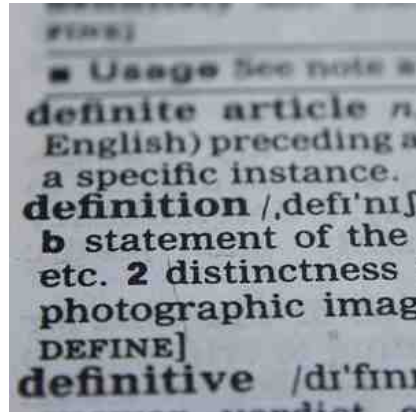




ISICEM15: SIRS and Sepsis: An Unhappy Marriage



What has been the impact of systemic inflammatory response syndrome (SIRS) on the definition of severe sepsis? Rinaldo Bellomo [(Melbourne, Australia), speaking at the International Symposium on Intensive Care and Emergency Medicine (ISICEM) in Brussels last month considered the validity of SIRS criteria in defining severe sepsis. Kaukonen, Bailey, Pilcher and colleagues including Bellomo have tested the sensitivity, face validity and construct validity of the SIRS criteria in defining severe sepsis, in the [recently published article](#) in the *New England Journal of Medicine* .

As Bellomo explained, in 1992 SIRS and sepsis got married, but it was a shotgun marriage, implying that there is this thing called SIRS that can be detected by looking at clinical characteristics. Even at the time, not everyone was happy with the marriage (for example, Vincent (1997) - [Dear SIRS, I'm sorry to say that I don't like you](#)).

Bellomo outlined some of the allegations:

- current terminology of “sepsis”, “infection” and “septicaemia” has enough problems
- SIRS is too sensitive, but is not specific
- SIRS does not reflect the severity of the disease process
- SIRS may detract from the search for infection

And yet SIRS criteria continue to dominate and are applied to patient recruitment in every sepsis trial. The criteria have poor specificity, as 82.2% of ICU patients without infection have “SIRS” criteria.

Looking at the validity of SIRS, Bellomo noted six criteria for validity:

1. Face validity - does the measure look like what is it intended to measure?
2. Concurrent validity - compares one tool's results with another measured at the same time points.
3. Criterion validity - compares the results of one tool against a gold standard.
4. Construct validity - degree to which the scores of an instrument are consistent with hypotheses (i.e. difference between relevant groups)
5. Predictive validity - the ability for an outcome measure to possibly predict another event.
6. Content validity - the degree to which the content of an instrument is an adequate reflection of the construct to be measured.

Bellomo explained the problems with SIRS criteria. Patients exist who have severe sepsis without SIRS (it has limited sensitivity in detecting patients who have severe sepsis), and who have features of major illness severity. Half who fulfil criteria of septic shock have different vital signs physiology on day 1.

To test the validity Bellomo and colleagues used 13 years of data from the ANZICS Adult Patient Database, specifically data on day 1 physiology, day 1 SIRS criteria, identification of infection and identification of sepsis in order to test the face validity of SIRS in defining sepsis, to test the construct, predictive and content validity of SIRS and the sensitivity of SIRS in identifying sepsis.

SIRS-negative patients have behaved the same way over 13 years:

- their outcome changes are identical
- their discharge destination changes over 13 years are identical
- there is no step-up in risk at two criteria (lack of construct validity).

Their study concluded that the need for two or more SIRS criteria to define severe sepsis excluded one in eight otherwise similar patients with infection, organ failure, and substantial mortality.

We need to demonstrate something special about two criteria, which is supposed to indicate SIRS-positive severe sepsis, suggested Bellomo.

There is no step up in risk after adjustment, and two criteria lack content and predictive validity. Concluded Bellomo, it's time for a divorce of SIRS and definition of sepsis.

Mervyn Singer (London, UK) concurred that SIRS is mortally wounded, Since the 2003 publication of sepsis definitions ("sepsis 2.0") there are registries, electronic health records and a better understanding of the pathophysiology of sepsis.

Singer is co-chair of the Sepsis Definitions Task Force, and shared what he emphasised are provisional thoughts from the Task Force about "Sepsis 3.0", which are awaiting endorsement and will be presented at the European Society of Intensive Care Medicine meeting in October 2015. "Crucially, we're proposing data-driven definitions - for the first time!" Singer noted.

The Task Force agrees that the host response is key, that sepsis is not simply a systemic inflammatory response, and that there are a variety of anti-inflammatory and other (mal)adaptive responses occurring concurrently. Sepsis should be defined as life-threatening organ dysfunction due to a dysregulated host response to infection. No-one liked the current definition, that sepsis is an infection and two or more of the systemic inflammatory response (SIRS) criteria, as it is too non-specific and can lead to over-diagnosis and over-prescription. There is agreement that sepsis represents "really sick" infection, an infection leading on to organ dysfunction and a bad outcome (ICU admission for organ support and possibly death). Therefore the Task Force is recommending that sepsis be defined as life-threatening organ dysfunction (characterised by a Sequential Organ Failure Assessment (SOFA) score ≥ 2 , due to a dysregulated host response to infection.

When it comes to defining septic shock, Singer acknowledged that variability rules, as a systematic review shows. Current thinking is that fluid-resistant hypotension requiring vasopressors, and elevated lactate have much higher mortality than either alone. Highly variable mortality rates from sepsis are reported, as they depend on the definition.

Christopher W. Seymour (Pittsburgh, USA) also addressed the issue of a reference standard for sepsis, stating that the real question in sepsis is who is "really sick" among those infected. The Task Force did not try to define infection or develop a "sepsis alert" for non-infected patients. To define infection, they used electronic health records to find first episodes of cultures and antibiotics (excluding prophylactic and intra-operative antibiotics) and to determine the date and time infection was first suspected. Using data from 836,895 patients they found that of these infection was first suspected 321,879 were infected at the ED, 384,22 in the ICU, 96,063 in the Ward and 34,731 elsewhere.

There are several ways to define 'really sick', including clinical review committees, if death occurs in the hospital, spending three or more days in the ICU, lots of organ dysfunction days later, or a discharge diagnosis of severe sepsis. The suggestion is to use a quick SOFA score (qSOFA) with three simple bedside criteria - altered mental status, respiratory rate and systolic blood pressure. As the majority of patients with infection are outside the ICU, qSOFA can identify easily those patients who

are “really sick”, possibly a 10-80 fold increase, according to Seymour. The qSOFA has been externally validated and analysed for sensitivity and is a superior tool on the ward and in the ED, concluded Seymour, although the Task Force expects and encourages debate.

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