BC Sepsis Network
Best Care, No Matter Where.

April 7, 2016

BC SEPSIS NETWORK SPECIAL COMMUNICATION ON THE THIRD INTERNATIONAL CONSENSUS DEFINITIONS FOR SEPSIS AND SEPTIC SHOCK (SEPSIS-3)

As many of you are aware, in February 2016, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) were published in JAMA.[i] The Sepsis-3 task force redefined the definitions of sepsis (removing severe sepsis from the definitions) and septic shock. The purpose of this work was to improve the clarity of the definitions not only for clinical care of patients but also for epidemiology, quality improvement and research.

Revised definitions for sepsis and septic shock

According to the revised definitions (see Table 1), "sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. For clinical operationalization, organ dysfunction can be represented by an increase from baseline in the Sequential [sepsis-related] Organ Failure Assessment (SOFA) (see Table 2) score of 2 points or more, which is associated with an in-hospital mortality greater than 10%." A SOFA score of 2 or greater identified a 2- to 25-fold increased risk of dying compared with patients with a SOFA score less than 2.

The consensus definitions also redefined septic shock "as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Patients with septic shock can be clinically identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater AND serum lactate level greater than 2 mmol/L in the absence of hypovolemia. This combination is associated with hospital mortality rates greater than 40%."

Table 1. Summary of Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

	New Definition	Clinical Operationalization
Sepsis (replacing severe sepsis)	Life-threatening organ dysfunction caused by a dysregulated host response to infection.	Organ dysfunction can be represented by an increase in the Sequential Organ Failure Assessment (see Table 1) score of 2 points or more, which is associated with an in-hospital mortality greater than 10%.
Septic Shock	A subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.	Identified by a vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater AND serum lactate level greater than 2 mmol/L in the absence of hypovolemia.

Table 2. Sequential (Sepsis-Related) Organ Failure Assessment Score (SOFA)

	Score				
System	0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: Fio_2, fraction of inspired oxygen; MAP, mean arterial pressure; Pao_2, partial pressure of oxygen.

[a] Adapted from Vincent et al.[27]

[b] Catecholamine doses are given as μg/kg/min for at least 1 hour.

[c] Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

Using quickSOFA scores to screen for sepsis

In out-of-hospital, emergency department, or general hospital ward settings, adult patients with suspected infection can be rapidly identified as being more likely to have poor outcomes typical of sepsis if they have at least 2 of the following clinical criteria that together constitute a new bedside clinical score termed quickSOFA (qSOFA):

- respiratory rate of 22/min or greater,
- altered mentation, or
- systolic blood pressure of 100 mm Hg or less.

In the cohort of patients used to derive the new definitions, among patient encounters with suspected infection outside the ICU (n = 66 522), qSOFA had high predictive validity for in-hospital mortality (AUROC, 0.81 [95% CI, 0.80-0.82]) that was statistically greater than that for SIRS (AUROC, 0.76 [95% CI, 0.75-0.77]), suggesting that it may have utility as a prompt to consider possible sepsis. This is not surprising as SIRS is often used to identify a new infection whereas a qSOFA score suggests clinical evidence of organ dysfunction. It is also important to realize that these prediction models do not consider how patients were treated that were identified with either SIRS or qSOFA.

The Sepsis-3 task force suggests that qSOFA criteria be used to prompt clinicians to:

- further investigate for organ dysfunction,
- initiate or escalate therapy as appropriate, and
- consider referral to critical care or increase the frequency of monitoring, if such actions have not already been undertaken.

The task force considered that positive qSOFA criteria should also prompt consideration of possible infection in patients not previously recognized as infected (similar to how we use SIRS criteria).

Removal of Systemic Inflammatory Response Syndrome (SIRS) criteria from definitions

The SIRS criteria have been removed from the official definition of sepsis and septic shock. The reason for this is that the SIRS criteria do not necessarily indicate a dysregulated, life-threatening response or sepsis. SIRS criteria are present in many hospitalized patients, including those who never develop infection and never incur adverse outcomes (poor discriminant validity).[ii] In addition, 1 in 8 patients admitted to critical care units in Australia and New Zealand with infection and new organ failure did not have the requisite minimum of 2 SIRS criteria to fulfill the definition of sepsis (poor concurrent validity) yet had protracted courses with significant morbidity and mortality.[iii] Discriminant validity and convergent validity constitute the 2 domains of construct validity; the SIRS criteria thus perform poorly on both counts.

Use of SIRS to identify new infections

Having said this, it is still believed that the SIRS criteria have utility in identifying new infections. The authors of the consensus definitions state:

> "nonspecific SIRS criteria such as pyrexia or neutrophilia will continue to aid in the general diagnosis of infection. These findings complement features of specific infections (eg, rash, lung consolidation, dysuria, peritonitis) that focus attention toward the likely anatomical source and infecting organism. However, SIRS may simply reflect an appropriate host response that is frequently adaptive. Sepsis involves organ dysfunction, indicating a pathobiology more complex than infection plus an accompanying inflammatory response alone."

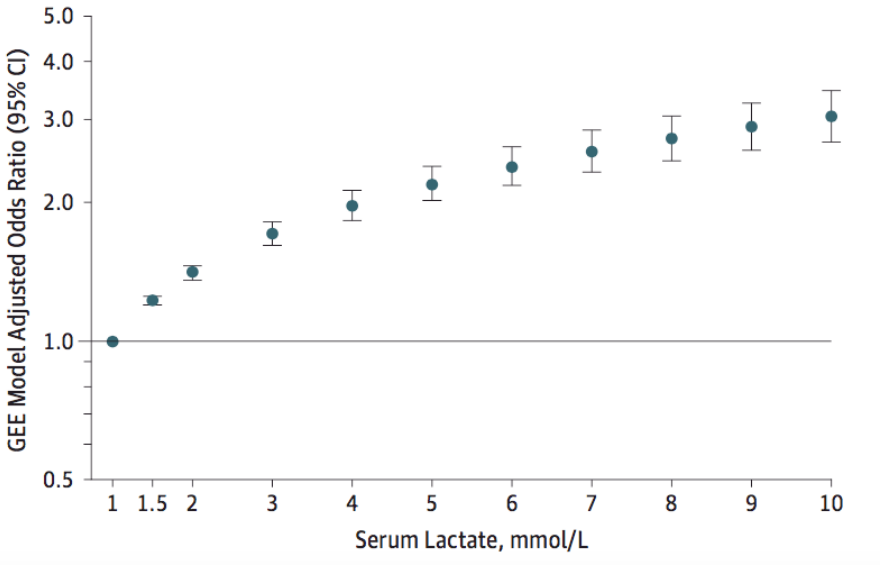
It is still believed that patients with a new infection and an appropriate host response still need identification and treatment to prevent the progression to sepsis/septic shock.

Impact on BC Sepsis Screening Algorithm

The new definitions, therefore, have little impact on the BC Emergency Department and In-Hospital Sepsis identification tools and preprinted orders as the purpose of these is to catch infections early and treat them before there is organ dysfunction. Therefore, SIRS is still used to help identify new infections and begin screening for organ dysfunction in both the ED and the in-hospital setting. In the new In-Hospital Sepsis identification tools (soon to be released by the BC Sepsis Network) we have included the qSOFA score in the tool/pre-printed order set as an indicator that further investigations may be required or that outreach/critical care consultation should be considered. We are holding off making changes to the BC Sepsis Guidelines until the publication of the 2016 Surviving Sepsis Guidelines (planned for this fall) as these new definitions (Sepsis-3) do not make any recommendations on the management of patients identified as being either septic or having septic shock.

Further, although an elevated lactate level is no longer included in the diagnosis of sepsis, the Sepsis-3 task force state that serum lactate level is associated with mortality, and the adjusted OR for hospital mortality increased linearly with increasing serum lactate level. An increase in serum lactate level from 2 to 10 mmol/L increased the adjusted OR for hospital mortality from 1.4 (95% CI, 1.35- 1.45) to 3.03 (95% CI, 2.68-3.45) (referent lactate = 1; Figure 1). Given this, we think it is important to keep a lactate level > 4.0 mmol/L as an additional indicator that mandates aggressive management in the ED and consideration of an outreach/critical care consult in the In-Patient setting.

Figure 1. Serum Lactate Level Analysis



Once the 2016 Surviving Sepsis Campaign Guidelines have been published (due to be released in Fall 2016), we will review all of our BC Sepsis Network resources and revise if necessary. As this work progresses, we will keep you posted on any changes and additions that affect our screening or processes of sepsis care in BC.

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References

[i] Singer M, et. al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). Journal of the American Medical Association. 2016; 315 (8): 801-810

[ii] Churpek MM, Zadravecz FJ, Winslow C, Howell MD, Edelson DP. Incidence and prognostic value of the systemic inflammatory response syndrome and organ dysfunctions in ward patients. Am J Respir Crit Care Med. 2015;192(8):958-964

[iii] Kaukonen K-M, Bailey M, Pilcher D, Cooper DJ, Bellomo R. Systemic inflammatory response syndrome criteria in defining severe sepsis. N Engl J Med. 2015;372(17):1629-1638