Diagnosis and management of sepsis

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Abstract. Sepsis is the life-threatening condition with organ dysfunction caused by dysregulated host response to the infection. Septic shock is part of sepsis where circulatory abnormalities and cellular metabolism occur. Sepsis and septic shock are still a problem in the world, where one in four people with sepsis will die. As well as any trauma case, acute myocardial infarction, or stroke, early identification and appropriate treatment of sepsis immediately after sepsis will improve the prognosis of the patient. Comprehensive management of septic patients is required, ranging from infection controls that include antibiotic administration and infection source control as well as hemodynamic stabilization that included fluid resuscitation and vasoactive drug delivery.

1. Definition

Sepsis is the life-threatening condition with organ dysfunction caused by dysregulated host response to the infection. Septic shock is part of sepsis where circulatory abnormalities and cellular metabolism occur. Septic shock hacharacterizationas hypotension, and after adequate fluid resuscitation, thepatientstill requires a vasopressor to maintain MAP ≥65mmHg, or blood lactate levels >2mmol/L. Sepsis and septic shock arestill a problem in the world, with one out of four people in sepsis will die. Identification of earlystage of sepsis and immediate management can improve the patient's prognosis.[1]

The Centers for Disease Control and Prevention (CDC) estimates that sepsis includes the top ten causes of overall mortality in the United States. Severe sepsis cause non-coronary death in ICU. Severe sepsis mortality rates reach 25% to 30% while septic shocks are up to 40% to 70%.[2]

2. Sepsis and Septic Shock Diagnostic Criteria

2.1. Sepsis

The clinical criteria for sepsis patients are using the Sequential (Sepsis-Related) Organ Failure Assessment (SOFA) score. SOFA score is easier to understand. SOFA score ≥2 is indicating organ dysfunction. Here is the SOFA score:

Table 1. Sequential [sepsis-related] organ failure assessment score.

	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

When infected, it is necessary to screen for the possibility of sepsis. This screening can be done anywhere and anytime. The method is by using quick SOFA (qSOFA). This scoring is considered stronger and simpler and requires no laboratory checks. Here are the qSOFA criteria:

Table 2. Quick SOFA (qSOFA) criteria.

Quick SOFA (qSOFA) criteria
1. Respiratory rate ≥22 times/minute
2. Consciousness change(Glasgow Coma Scale's score ≤13)
3. Systolic blood pressure ≤100 mmHg

The qSOFA score is defined as positive if there are 2 from 3 criteria above. These scores can be used quickly by clinicians to determine the presence of organ dysfunction, to initiate appropriate therapy, and as a consideration for referring to critical care or improving surveillance. If qSOFA score is positive, then the condition will be scored by the SOFA method.[3]

2.2. Septic Shock

Patients with septic shock may be identified by theclinical manifestation of sepsis with persistent hypotension which requires vasopressors to maintain MAP ≥65 mmHg and lactate serum levels higher than 2mmol/L (18mg/dL) despite adequate resuscitation volume. With this criterion, the risk of death in the hospital is more than 40%.[3]

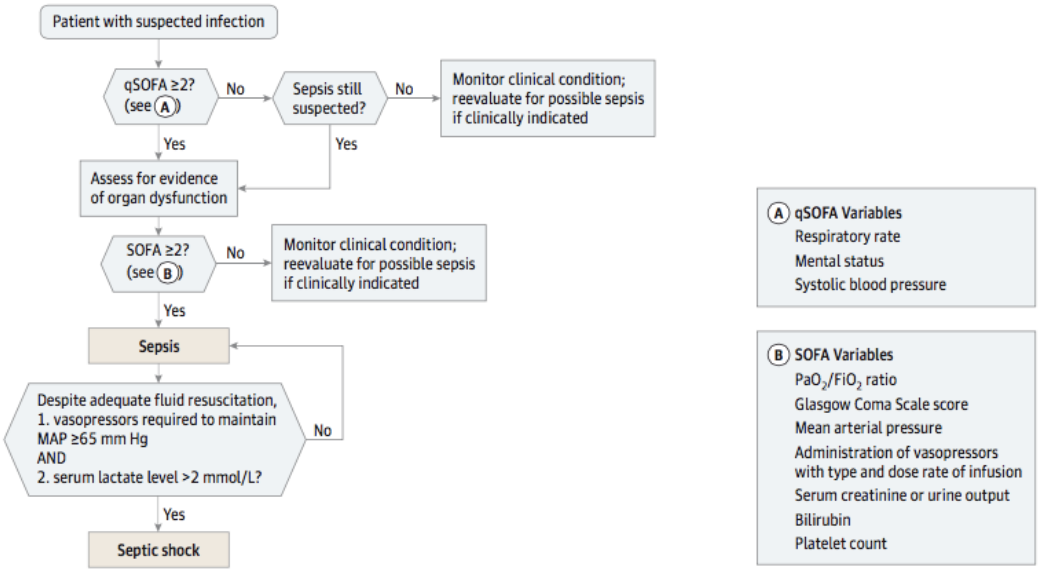

Figure 1. The algorithm of sepsis.

3. Sepsis Management

Management of the patient with septic involves three components: treatment of the infection, cardiovascular resuscitation, and immunomodulation. Control infection using adequate antibiotics and source control. When hemodynamic stabilization was performed by fluid resuscitation and vasoactive drug administration.[4]

3.1. The principle of antibiotic therapy in sepsis

Intravenous antimicrobial administration begins as soon as possible within the first hour after the patient is known to have sepsis and septic shock. The sooner antimicrobial administer of the patient will determine the success of the therapeutic effect. In circumstances where sepsis or septic shock is present, delaying antimicrobial administration every hour can lead to an increased risk of death. Furthermore, some studies have demonstrated the presence of undesirable acute kidney injury (AKI), acute lung injury (ALI), and other organ damage due to antimicrobial delay in patients.[1]

Broad-spectrum empirical therapy is the recommendation with one or more antimicrobials for septic or septic shock. Failure to initiate appropriate empirical therapy in patients with sepsis and septic shock associated with increased morbidity and mortality. Thus, the initial selection of antimicrobial therapy should be broad enough to cover all possible pathogens (bacteria, fungi, viruses). The choice of empirical antimicrobial therapy depends on the patient's history of the disease, the source of the infection, the accompanying illness, the infection obtained from the community or the healthcare establishment. If the culture of sensitivity has a result, adjust antimicrobial therapy immediately.[1]

3.2. The principle of fluid therapy in sepsis

In the human body, the liquid can be divided according to its location, i.e., intracellular and extracellular. The extracellular fluid itself can bedivided into interstitial fluid and intravascular fluid. The fluid exchange occurs in areas where there are large capillary and venous blood vessels. The membranes of the capillaries and venules are semipermeable, so fluid from extracellular can move to intracellular, and vice versa. The amount of fluid and electrolyte present in the plasma must achieve a balanced and optimal state, called as homeostasis.[5]

Recent research suggests that there is a layer that limits plasma in blood vessels with capillary vascular endothelium called glycocalyx. This glycocalyx layer lies in the endothelial cells and serves

to filter out plasma proteins that can move to endothelial cells. Also, glycocalyx serves to inhibit leukocyte and platelet aggregation. Sepsis conditions can damage Glycocalyx. When this layer is broken, the plasma protein filter is also broken, and plasma "leaks" to the endothelial cells will then continue to the interstitial tissue, causing interstitial edema.[5]

Resuscitation fluids are colloidal and crystalloid fluids. Colloidal fluid means the suspension of molecules contained in the liquid, has a greater molecular weight, and can not penetrate the semipermeable membrane of capillary blood vessels. While the crystalloid liquid consists of ions that can penetrate the semipermeable membrane of capillary blood vessels, and contain sodium and chloride. Each resuscitation fluid has the advantage or the advantages of each to achieve the required resuscitation goals.[6]

Colloidal fluid is more effective in increasing intravascular volume because colloid fluid cannot penetrate the semipermeable membrane of capillary blood vessels so that it will remain in the blood vessels. The crystalloid liquid is cheaper than the colloidal fluid and has the same effect. However, the use of crystalloid fluid for too long can cause edema of the interstitial tissue, due to the crystalloid liquid content that can penetrate the semipermeable membrane, resulting in the possibility of thefluidstored in the interstitial tissues.[6]

The latest Guideline Surviving Sepsis Campaign recommends 30ccs/kgBB crystalloid administration within the first 3 hours. During the administration of fluids should always be evaluated the adequacy of fluids in the body. If it has reached 30ccs/kgBB in 3 hours the patient still needs more fluids, then it is recommended the use of low concentration albumin (4-5%). Whereas if not yet reached 30ccs/kgBB there have been signs of fluid overload, e.g., shortness of breath, rales on auscultation examination of lung fluid resuscitation need to stop immediately.[7]

The principle of aggressive administration of fluids in sepsis such as the Elderly Goal Directed Therapy (EGDT) protocol by Emanuel Rivers with a target of 8-12 cmH2O CVP is no longer a recommendation. Aggressive fluid resuscitation will lead to adverse consequences of increased heart fill pressure, damage to endothelial glycocalyx, arterial vasodilation,and tissue edema. Administration of aggressive fluid resuscitation increases the morbidity and mortality of septic patients.[7, 1]

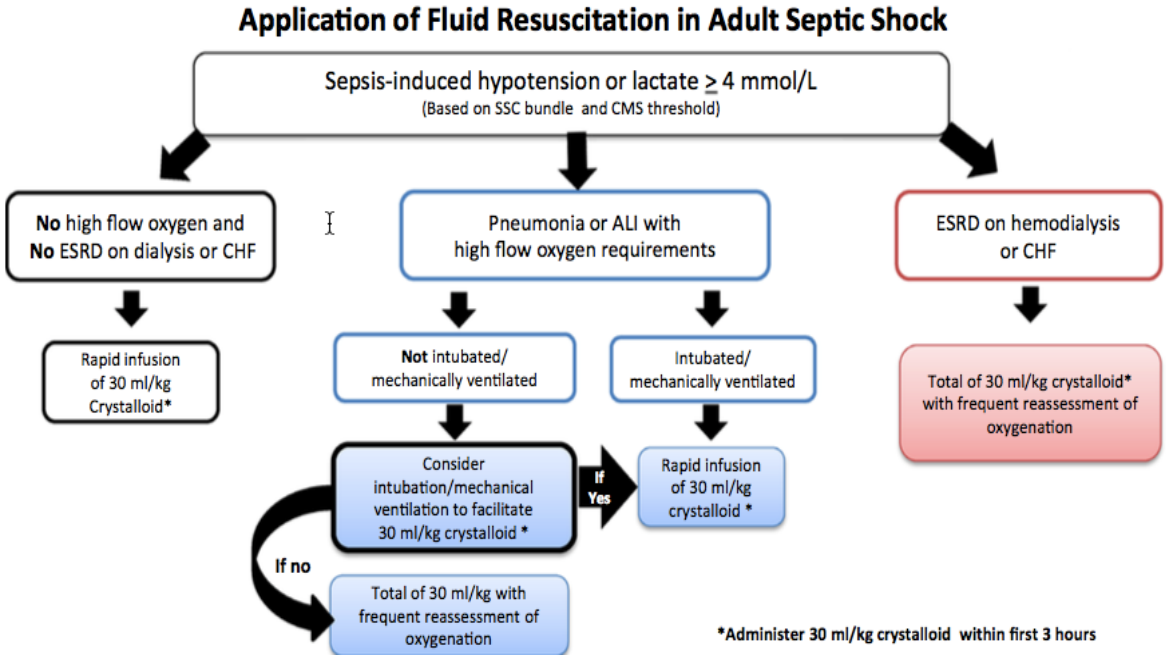

Figure 2. The application of fluid resuscitation in adult septic shock [7].

The purpose of resuscitation is to improve the perfusion of oxygen to the tissues, resulting in a balance between flowing oxygen and consuming the oxygen. One of the parameters to know perfusion to adequate tissue is to maintain the Mean Arterial Pressure (MAP) pressure of up to 65 mmHg. Use norepinephrine as a first-line vasopressor to improve theMAP. Norepinephrine fixes preload, systemic vascular resistance,and cardiac output. Its use in patients with persistent hypotension is a recommendation early in the course of septic shock. Perform fluid resuscitation first, if the target MAP has not been achieved just use norepinephrine.[1]

Passive Leg Raising (PLR) maneuvers and fluid bolus tests coupled with real-time SV monitoring are currently the only technique for knowing acceptable clinical accuracy to determine fluid adequacy. The PLR maneuver needs for lifting the leg passively from a horizontal position. This maneuver will provide a blood flow of about 300 ml from the lower extremities and the abdomen to the intrathoracic compartment. It is easy using this method, and the accuracy is very high to determine the adequacy of fluids.[6]

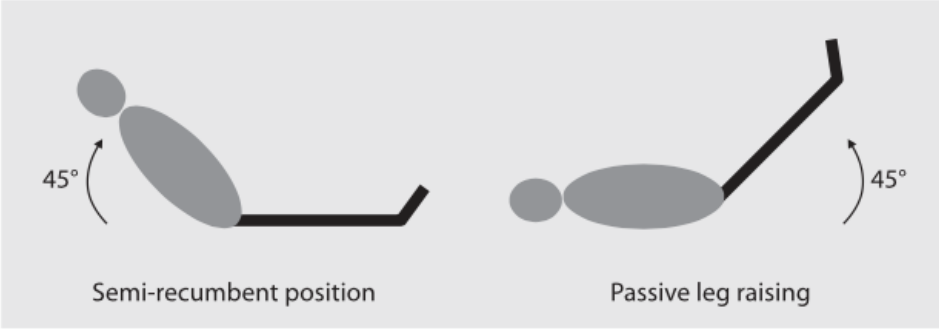

Figure 3. PLR technique is done about 30 seconds.

Monitor fluids should be more strict in sepsis patients. Monitor fluids should be done every day and calculated cumulatively every day. Because if not done cumulative summation often error what amount of fluid that has been given and will be difficult to do the correction. Excess 1 liter of fluid lasting for 24 hours will increase 20% risk of patient death.[8]

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