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Chawika Pisitsak
Keith R. Walley

Does this patient have septic shock?

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C. Pisitsak · K. R. Walley (✉)
Centre for Heart Lung Innovation, University of British Columbia, Vancouver, BC V6Z 1Y6, Canada
e-mail: Keith.Walley@hli.ubc.ca
Tel.: (604) 806-8136

C. Pisitsak
Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

K. R. Walley
HLI, St. Paul's Hospital, 1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada

The diagnosis of septic shock is typically not straightforward since sepsis presents with an array of clinical features and very frequently occurs in the context of other disease states. Rapid diagnosis of septic shock requires both an approach to the differential diagnosis of shock and an approach to the diagnosis of sepsis. Interestingly, the clinical history is often the most specific clinical feature.

Is this patient in a shock state?

Shock is circulatory failure resulting in inadequate oxygen delivery to vital organs leading to impaired organ function due to tissue hypoxia. Accurate initial diagnosis and classification of shock can greatly affect outcome.

Hypotension is the most common feature of shock but, by itself, is neither sensitive nor specific. A systolic blood pressure of less than 90 mmHg or the mean arterial pressure of less than 65 mmHg or a decrease of systolic blood pressure from baseline more than 40 mmHg are guidelines to aid in diagnosis [1]. In addition to blood pressure criteria, it is essential to seek accompanying clinical signs of poor organ perfusion and function, e.g., altered mentation, oliguria, delayed capillary refill, and cold, cyanotic, mottled skin. Lactate and central venous oxygen measurement can assist the detection of inadequate tissue perfusion. A lactate level of more than 4.0 mmol/L is associated with increasing mortality even in normotensive patients [2] and, therefore, has been proposed as an alternative clinical feature defining shock that can be used to trigger shock treatment protocols [3]. However, an elevated lactate level may be due to reasons other than shock, e.g., endogenous or exogenous catecholamines or impaired hepatic clearance of lactate [4]. Furthermore, even a lactate level in the high-normal range is associated with increased mortality. Thus, no single clinical feature defines shock. Concordance among multiple clinical features is diagnostic (e.g., history, vital signs, organ dysfunction, lab values, presence of an underlying cause).

Differential diagnosis of shock at the bedside

A practical mnemonic to aid in the differential diagnosis of shock is SHOCK: S = *S*eptic/distributive shock, H = *H*ypovolemic shock, O = *O*bstructive shock, C = *C*ardiogenic shock, and K = (*K*) combinations or (rare) *K*inds. A rapid clinical approach to arrive at a working diagnosis is to proceed stepwise through this differential diagnosis by addressing four questions (Table 1). First, "Is cardiac output high or low?" If cardiac output is normal or high (not low), then distributive shock (most commonly septic) is likely. In septic shock,

Table 1 Differential diagnosis of shock using clinical assessment

1. Is cardiac output high or low?	Normal or high cardiac output (**S**HOCK)	Low cardiac output (S**HOC**K)
Physical examination		
Quality of pulse	Strong	Weak
Pulse pressure	Increased	Decreased
Extremities	Warm	Cool
Capillary refills	Less than 2 s	More than 2 s
Evidence of infection or major tissue injury (e.g., trauma, pancreatitis)	Present	Absent
Objective measurement		
Cardiac output measurement: indicator dilution, pulse contour analysis, esophageal Doppler, echocardiography, bioimpedance or bioreactance, mixed venous oxygen saturation (Fick equation)	Normal or high cardiac output measurement	Low cardiac output measurement

2. Is the circulation full?	No (S**H**OCK)	Yes (SH**OC**K)
Physical examination		
Jugular veins	Flat	Distended
Heart sounds	Normal	Possible S3, S4, rub
Dependant edema	Absent	Present
Skin	Poor skin turgor	Edema
Objective measurement		
Chest X-ray	Clear lungs	Pulmonary congestion Large cardiac silhouette
Static preload assessment	Low CVP, low PCWP	High CVP, high PCWP
Dynamic preload assessment: fluid responsiveness	Mechanically ventilated: PPV $\geq$ 13 % [17] SVV $\geq$ 12 % [17]	Minimal change with respiration
	Response to passive leg raising	No response to passive leg raising
Goal-directed echocardiography	Mechanically ventilated: dIVC $\geq$ 18 % [18] Spontaneous breathing: collapsing IVC with respirations Small, hyperdynamic ventricles	Full and non-collapsing IVC Dilated, poorly contractile cardiac chambers

3. Are the lungs clear?	Yes (SH**OC**K)	No (SHO**C**K)
Physical examination		
Breath sound differences between obstructive and cardiogenic shock	Clear (tamponade) Absent unilaterally (pneumothorax)	Crackles
Heart sounds	Loud P2 (pulmonary embolus) Faint (tamponade)	S3, S4, murmur
Objective measurement		
Chest X-ray differences between obstructive and cardiogenic shock	Clear lungs	Pulmonary congestion Large cardiac silhouette
Goal-directed echocardiography	Distended right heart, right-to-left septal shift (pulmonary embolism) Pericardial effusion (tamponade)	Decreased ventricular contractility Regional wall motion abnormality
	⇓	
4. What does not fit?	(K) combinations (septic + cardiogenic, septic + hypovolemic, etc.) Rare kinds of shock	

The underlying letter(s) in the SHOCK mnemonic indicate the type of shock (Septic, Hypovolemic, Obstructive, Cardiogenic)
If cardiac output is high then distributive (commonly septic) shock is likely
If cardiac output is low then proceed to question 2. If the circulation is not full then hypovolemic shock is likely. If the circulation is full then proceed to question 3. If the lungs are clear then obstructive shock should be considered. If the lungs are not clear then cardiogenic shock is likely
CVP central venous pressure, *PCWP* pulmonary capillary wedge pressure, *IVC* inferior vena cava, *PPV* pulse pressure variation, *SVV* stroke volume variation, *dIVC* IVC distensibility index

diastolic arterial pressure, which physiologically reflects the arterial tone, is typically decreased. Arterial pulse pressure, which is related to stroke volume, is typically normal or high (Table 1). Mixed or central venous oxygen saturation can be elevated. In contrast, if cardiac output is low, the physician should proceed to the second question: "Is the circulation full or not?" Flat jugular veins, decreased tissue turgor, and a mechanism

explaining volume loss (bleeding, diarrhea, etc.) point towards hypovolemic shock. Alternatively, if the patient has increased jugular venous pressure and other evidence of a full circulation such as edema, then proceed to the third question: "Are the lungs clear?" In the setting of low cardiac output with elevated jugular veins, crepitation on lung auscultation, and classical chest x-ray findings, then cardiogenic shock is most likely. Clear lungs in this setting suggest the diagnosis of obstructive shock; most commonly massive pulmonary embolism, cardiac tamponade, or tension pneumothorax. Bedside goal-directed echocardiographic examination is particularly helpful in addressing this third issue [5].

The fourth question that should always be asked is "What doesn't fit?" When the first three questions do not lead to a clear conclusion then a combination of different types of shock should be considered. This is particularly important in septic shock because it almost always presents with a significant component of hypovolemia and is often accompanied by septic cardiomyopathy mimicking a cardiogenic profile. The right ventricle may also be involved in septic cardiomyopathy. Goal-directed echocardiography directly addresses these issues so is particularly helpful in this setting. When accompanying hypovolemia is treated with initial fluid resuscitation, a clear clinical diagnosis of septic shock may emerge. When the clinical features still do not fit a diagnosis, rare types of shock must be entertained (e.g., adrenal insufficiency, neurogenic shock, etc.).

Is this patient septic?

Sepsis is a systemic inflammatory response (SIRS) due to known or suspected infection [6]. It follows that key initial steps include culture and, where appropriate, microscopic examination of sputum, urine, blood, and other fluids and tissues to define a known infection. In many cases cultures remain negative, so defining infection remains a clinical judgment. Use of two or more classical SIRS criteria (temperature, heart rate, respiratory rate, white blood cell count) in the definition of sepsis has been helpful but is an oversimplification. To improve specificity to differentiate between patients with septic SIRS or non-septic SIRS (severe pancreatitis, burns, or trauma), adding more clinical parameters and biomarkers may be useful [7]. Accordingly, in the latest "International Guidelines for Management of Severe Sepsis and Septic Shock: 2012" the diagnostic criteria for sepsis are documented or suspected infection with criteria from the categories of (1) general variables (vital signs, mental status, fluid balance, glucose), (2) inflammatory variables (white blood cell count and plasma biomarkers), (3) hemodynamic variables (blood pressure), (4) organ dysfunction, and (5) tissue perfusion variables (lactate, capillary refill) [8].

Biomarkers

In view of the clinical challenges in sepsis diagnosis, interest in sepsis biomarkers has increased. None of the biomarkers studied to date are particularly sensitive and specific. Elevated plasma C-reactive protein (CRP) and procalcitonin more than two standard deviations above normal values may be helpful [8]. However, CRP can increase in inflammatory states unrelated to sepsis. Procalcitonin is more specific for bacterial infection [9, 10]. Measurement of 1,3-beta-D-glucan, mannan, and antimannan antibody may assist in the diagnosis of fungal infection [8]. Other biomarkers, e.g., patterns of pro-inflammatory cytokines, gene expression in specific sepsis related-pathways, pathogen and host DNA, and human genetic variants [11] are currently under investigation. Rather than looking at one specific biomarker, physicians should combine multiple clinical, imaging, and laboratory parameters to help diagnose sepsis.

The most important step

After rapid bedside diagnosis of septic shock, prompt treatment is crucial. Early recognition, early appropriate antibiotics administration, early volume and hemodynamic resuscitation using vasopressors, and organ support are transformative in improving outcomes [12]. In life-threatening cases all of these interventions can be initiated in parallel. It should be noted that septic shock is very frequently diagnosed a posteriori, i.e., after fluid resuscitation fails to fully reverse the hemodynamic deficits. In 2001, Rivers et al. [13] found that protocolized resuscitation markedly improves mortality in severe sepsis and septic shock. Many additional studies confirm the benefit of protocolized resuscitation. Recently, three major RCTs (ARISE, ProCESS, and ProMISe) used protocolized identification and resuscitation of patients and uniformly found surprisingly low mortality rates for septic shock. They further found that a variety of approaches to evaluating adequacy of volume resuscitation and adequacy of oxygen delivery were just as good as the specific approaches studied by Rivers et al. many years ago [14–16].

Conclusions

A rapid bedside diagnostic approach to shock (mnemonic SHOCK) combined with a knowledge of clinical features of sepsis (categories include general, inflammatory, hemodynamic, organ dysfunction, and tissue perfusion) leads to a rapid diagnosis of septic shock. Early

administration of antibiotics and rapid protocol-driven resuscitation are instrumental in leading to good clinical outcomes.

Compliance with ethical standards

Conflicts of interest No authors have conflicts of interest relevant to this manuscript.

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