Integrated Multiorgan Bedside Ultrasound for the Diagnosis and Management of Sepsis and Septic Shock

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Abstract

Despite decades of research, the mortality rate of sepsis and septic shock remains unacceptably high. Delays in diagnosis, identification of an infectious source, and the challenge of providing patient-tailored resuscitation measures routinely result in suboptimal patient outcomes. Bedside ultrasound improves a clinician's ability to both diagnose and manage the patient with sepsis. Indeed, multiple point-of-care ultrasound (POCUS) protocols have been developed to evaluate and treat various subsets of critically ill patients. These protocols mostly target patients with undifferentiated shock and have been shown to improve clinical outcomes. Other studies have shown that POCUS can improve a clinician's ability to identify a source of infection. Once a diagnosis of septic shock has been made, serial POCUS exams can be used to continuously guide resuscitative efforts. In this review, we advocate that the patient with suspected sepsis or septic shock undergo a comprehensive POCUS exam in which sonographic information across organ systems is synthesized and used in conjunction with traditional data gleaned from the patient's history, physical exam, and laboratory studies. This harmonization of information will hasten an accurate diagnosis and assist with hemodynamic management.

Keywords
- POCUS
- bedside ultrasound
- sepsis
- septic shock

Sepsis and, in particular, septic shock is a medical emergency in which early diagnosis and timely treatment with antibiotics is associated with improved outcomes.[1] Unfortunately, the clinical diagnosis of sepsis can be challenging as patients can present with a disparate range of vital signs (fever or hypothermia), physical exam findings, (warm or cool extremities) or basic laboratory measures (leukocytosis or leukopenia). Troponin and lactate values can be especially difficult to interpret in acutely ill patients, as both can be elevated in either sepsis or a variety of cardiac conditions.[2,3] Novel biomarkers have not resolved this diagnostic dilemma; although more than 30 biomarkers of sepsis have been identified and tested, none have proven worthy of routine clinical use.[4] Further complicating the clinical presentation of sepsis is the paramount importance of early and effective control of the source of infection.[5] Traditional findings of the history, physical exam, and laboratory measure may prove nonspecific and the use of advanced imaging modalities such at computed tomography (CT) or magnetic resonance imaging (MRI) may not be feasible due to the hemodynamic instability of the critically ill patient.

The clinical challenge of early and accurate identification of sepsis and the underlying infection created an opportunity for the development of point-of-care ultrasound (POCUS) as an effective and feasible bedside diagnostic modality. As early as 1993, Lichtenstein and colleagues demonstrated the use of a comprehensive, whole-body bedside ultrasound examination for the initial assessment of a critically ill patient.[6,7] In an early observational study of 150 consecutive ICU patients, a whole-body POCUS impacted the therapeutic plan in 22% of patients, including identifying a source of infection in 15% of all patients.[6] A more contemporary study

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Table 1 Components of published ultrasound protocols for the assessment of shock

Protocol (year of publication)	FATE (2004)	ACES (2009)	RUSH: HIMAP (2009)	RUSH: Pump, Tank, Pipes (2009)	EGLS (2011)	FALLS (2012)	POCUS (2012)
Cardiac	X	X	X	X	X	X	X
IVC		X	X	X	X	X	X
FAST A/P		X	X	X			X
Aorta		X	X	X			X
Lungs PTX			X	X	X	X	X
Lungs effusion	X	X		X			
Lungs edema				X	X	X	X
DVT				X			X
Ectopic pregnancy							X

Abbreviations: DVT, deep vein thrombosis; FAST A/P, focused assessment with sonography for trauma abdomen and pelvis; IVC, inferior vena cava; PTX, pneumothorax.
Source: Modified from Seif et al (Distributed under the Creative Commons Attribution License).[9]

of 200 patients meeting Surviving Sepsis Campaign criteria for sepsis demonstrated that POCUS evaluation in the emergency room was superior to a standard initial clinical assessment (history and physical exam; and basic laboratory testing) for the identification of the source of infection.[8] Bedside ultrasound performed by highly trained emergency medicine physicians improved the clinical diagnostic accuracy for an infectious source from 52.5 to 75%.

In addition to its diagnostic value, POCUS can be beneficial in guiding treatment by allowing the provider to tailor therapies to optimize patient hemodynamics. For example, patients with ventricular dysfunction due to underlying cardiomyopathy or sepsis-induced cardiomyopathy (SCM) require a different clinical approach than patients with septic shock and preserved cardiac function. Multiple protocols have been developed that utilize POCUS for rapid assessment of hemodynamics to direct the diagnosis and treatment of shock (►**Table 1**).[9] Among critically ill patients with undifferentiated shock, there is evidence to suggest that management guided by bedside cardiac ultrasound is beneficial. In a retrospective study of 110 patients with subacute shock, those managed with limited cardiac ultrasound received less fluid resuscitation (49 vs. 66 mL/kg in the first 24 hours, $p = 0.04$) and relatively more inotropic support (dobutamine 22 vs. 12%, $p = 0.01$) compared with historic controls.[10] Moreover, bedside ultrasound-guided therapy was associated with a higher 28-day survival rate compared with controls (66 vs. 56%, $p = 0.04$). Additional studies specifically involving patients with septic shock suggest a mortality benefit when formal echocardiography is performed.[11,12] These data are promising, as they highlight the potential clinical impact of bedside cardiac ultrasound in the assessment of critically ill patients when performed by experienced practitioners.

Undoubtedly, there are limitations to the role of POCUS in the diagnosis and management of sepsis and septic shock. Indeed, ultrasound training remains inconsistent across emergency medicine and, to a larger degree, critical care medicine.[13] POCUS is not a replacement for conscientious history-taking, comprehensive physical exam, and thoughtful analysis of laboratory data in the assessment of a patient with possible sepsis. Rather, POCUS should be viewed as a valuable adjunct in both the diagnosis and management of sepsis and septic shock.

POCUS and the Diagnosis of Sepsis, Septic Shock, and Source of Infection

The POCUS exam for sepsis or septic shock should be systematic and integrate the assessment of multiple organ systems. This comprehensive approach improves the provider's ability to diagnose the presence of sepsis or septic shock and identify the culprit infection. Additionally, POCUS can serve to narrow down the differential diagnosis in challenging cases and provide important information to identify concomitant pathology or alternative diagnoses.

Cardiac Assessment

Cardiac ultrasound provides noninvasive evaluation of cardiac anatomy as well as cardiac and systemic hemodynamics. Ideally, the cardiac ultrasound exam should utilize several acoustic windows to provide a reasonable assessment of valvular and biventricular function (►**Fig. 1**). Common protocols begin in the parasternal window with both long- and short-axis views of the left ventricle (►**Fig. 1A, B**). The parasternal long-axis view allows evaluation of left ventricular size/function and quick assessment of the mitral and aortic valves. The parasternal short-axis view provides a more focused view of left ventricular systolic function and is good for the assessment of regional wall motion abnormalities (RWMAs). In the apical four-chamber view, biventricular systolic function can be assessed as well as right ventricular enlargement so long as the image is not foreshortened, which occurs if the ultrasound plane does not pass through the apex of the heart (►**Fig. 1C**). Mitral and tricuspid valves are also well seen in this view. Finally, the

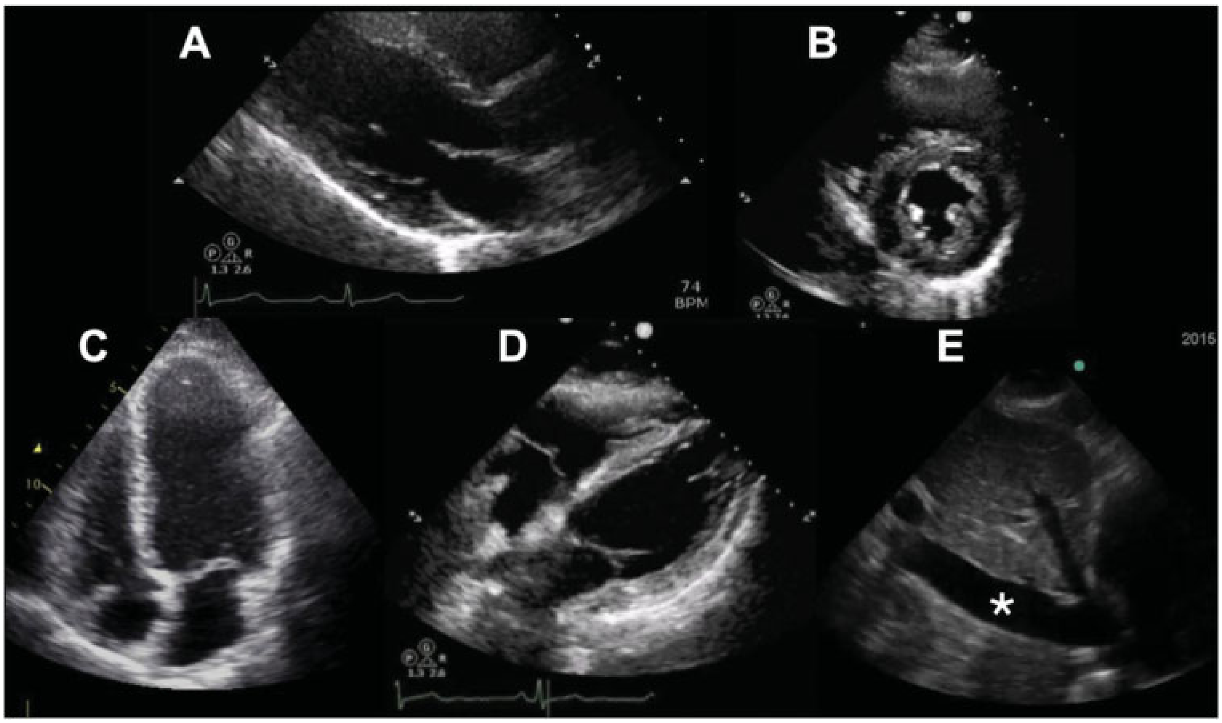

Fig. 1 The images detail the four basic views for the assessment of cardiac anatomy and function. The integration of these views allows the evaluation of biventricular function, cardiac valves, and pericardium. (**A**) Parasternal long axis, (**B**) parasternal short axis, (**C**) apical four-chamber, (**D**) subcostal, (**E**) subcostal view showing inferior vena cava (*).

subcostal window is excellent for detecting the presence of a pericardial effusion or right ventricular enlargement and if the probe is rotated 90 degrees then the inferior vena cava (IVC) can be visualized entering the right atrium (►**Fig. 1D**).

Accurate qualitative evaluation of biventricular systolic function and estimation of left ventricular ejection fraction (LVEF) can be adequately performed by noncardiologists and is important for the management of patients presenting in septic shock.[14–16] Although septic shock is classically characterized by vasodilatory physiology with preserved or hyperdynamic left ventricular systolic function, there is also a subgroup that will present with reduced LVEF secondary to SCM (►**Fig. 2A**).[17] The prevalence of SCM varies from 10 to 70% depending on the definition. When the diagnosis of SCM mandates an LVEF less than 45%, the prevalence of SCM remains substantial, occurring in 30 to 50% of all patients with septic shock. However, it is important to recognize that many patients may have reduced LVEF at baseline due to underlying ischemic cardiomyopathy (ICM), which can be exacerbated by sepsis and septic shock. Furthermore, patients with coronary artery disease and normal cardiac function at baseline may develop dynamic changes in LVEF due to cardiac ischemia in the setting of sepsis and septic shock. Whether cardiac ischemia or a preexisting cardiomyopathy is caused by left ventricular dysfunction in an undifferentiated septic patient is often not easily delineated. The hallmark of cardiac ischemia is RWMAs that correspond to coronary artery vascular distribution. SCM tends to differentiate itself from ICM by presenting with a more global or generalized pattern of ventricular hypokinesis. Furthermore, there is an important subset of patients that develop nonischemic stress-induced cardiomyopathy, commonly referred to as Takotsubo cardiomyopathy (►**Fig. 2B**).[18] Takotsubo cardiomyopathy classically presents with impaired contractility of the apex that can extend into midsegments of the left ventricle. This RWMA pattern has been termed "apical ballooning" as there is usually hypercontractility of the base of the left ventricle. The pattern of

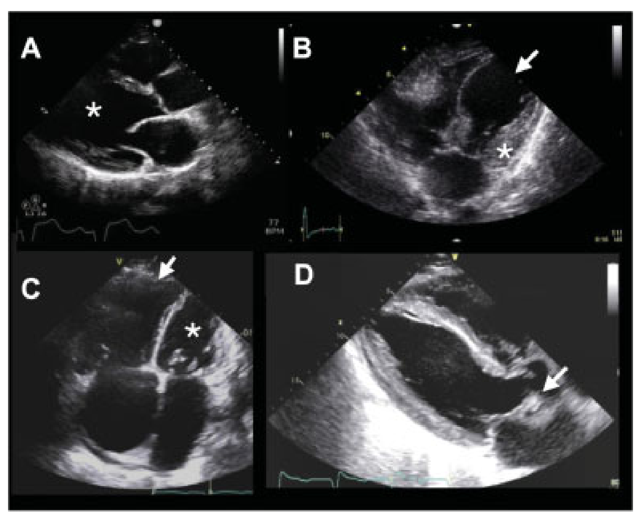

Fig. 2 Cardiac ultrasound pathology and shock. (**A**) Dilated left ventricle (*) with reduced ventricular systolic function secondary to either chronic cardiomyopathy or septic cardiomyopathy. (**B**) Takotsubo cardiomyopathy with apical "ballooning" (arrow) and compensatory basal hyperkinesis (*). (**C**) Severely dilated right ventricle and right atrium (arrow) consistent with severe right ventricular failure. Note that left ventricle is compressed and small (*). (**D**) Thickened, abnormal aortic valve (arrow) consistent with endocarditis.

RWMA seen with Takotsubo cardiomyopathy extends beyond the vascular distribution of a single epicardial artery, which helps differentiate this acute non-ICM from ICM. Additional findings that can be suggestive of ICM as opposed to non-ICM include left ventricular dilation with eccentric hypertrophy or focal thinning of ventricular wall segments and left atrial dilation. Moreover, SCM and Takotsubo cardiomyopathy, unlike ICM, demonstrate reversibility with eventual resolution of the ventricular dysfunction.[17] However, it is important to note that multivessel coronary artery disease can demonstrate a RWMA pattern similar to Takotsubo cardiomyopathy and therefore coronary angiography is necessary for definitive diagnosis.

The right ventricle should also be evaluated in patients who present with suspected sepsis or septic shock (►**Fig. 2C**). Isolated right ventricular dysfunction is not considered a classic feature of septic shock or SCM. However, right ventricular dysfunction either isolated or in combination with left ventricular dysfunction is a relatively common occurrence with severe sepsis or septic shock and the etiology may be multifactorial due to hypoxemia, hypercapnia, acidosis, or mechanical ventilation.[19] Importantly, the presence of right ventricular dysfunction in the setting of severe sepsis or septic shock is associated with increased mortality.[19,20]

Cardiac valves warrant evaluation in the setting of sepsis or septic shock. Although comprehensive interrogation of valvular function is beyond the scope of bedside ultrasound, the ability to identify the presence of severe valvular dysfunction has important clinical value as it helps direct the resuscitation and stabilization of critically ill patients. Additionally, endocarditis can be suggested by the presence of amorphous echogenic masses, associated with the cardiac valves, which demonstrate independent motion (►**Fig. 2D**).[21] Severe cases of endocarditis usually result in leaflet destruction and valvular incompetence (regurgitation). It is important to note that formal transthoracic echocardiography has limited sensitivity in high-risk patients such as those with prosthetic cardiac valves or devices, congenital heart disease, or prior history of endocarditis and as a result, transesophageal echocardiography is usually recommended in these cases.[22]

The bedside cardiac ultrasound exam also includes evaluation of the pericardium. Although the pericardium can be visualized in the four basic cardiac ultrasound views, the subcostal acoustic window is usually the best view for the detection of a pericardial effusion. It is important to rule out the presence of a pericardial effusion in hypotensive patients as tamponade is a critical condition that can be reversed with prompt intervention. Notably, the development of tamponade physiology does not require the presence of a large effusion and impaired cardiac hemodynamics can occur with rapid accumulation of relative amount of fluid into the pericardial space. If a pericardial effusion is present, the characteristics of the fluid should be assessed. Simple transudative fluid appears anechoic and homogeneous. The presence of heterogeneous appearing fluid with stranding or mobile debris suggests an exudative etiology or chronicity.[23]

The IVC is a component of the cardiac bedside ultrasound exam and can be interrogated in the subcostal acoustic window. The IVC provides insight into volume status and right atrial pressure that can be utilized for guiding therapy and will be addressed later in this article.

Pulmonary Assessment

Lung ultrasound (LUS) is a high-yield diagnostic modality for sepsis and septic shock. LUS technique utilizes patterns of sonographic artifacts to evaluate for pleural and subpleural abnormalities. In normally aerated lung, only the pleural lining is visible by ultrasound (►**Fig. 3A**). The pleural line (consisting of both the visceral and parietal pleura) appears hyperechoic, thin, and smooth. An irregular and thickened pleural line is sometimes seen in fibrotic lung disease (►**Fig. 3B**). As lung density increases, due to interstitial thickening (due to edema or fibrosis) or alveolar consolidation (frequently termed "alveolar-interstitial syndrome"), bright vertical reverberation artifacts originating from the pleural line begin to appear. These reverberation artifacts are termed "B-lines" and extend the length of the ultrasound image (►**Fig. 3C**).[24] The number of B-lines increases in parallel with increased lung density due to pulmonary edema or interstitial pathology. Unilateral B-lines isolated to a specific region of the lung and sometimes associated with a subpleural hyperechoic irregular border ("shred sign") can suggest a focal process such as pneumonia (►**Fig. 3D**). On the other hand, diffuse B-lines visualized bilaterally across the chest in clinical setting of left ventricular dysfunction and dyspnea is indicative of congestive heart failure. The presence of bilateral pleural effusions further solidifies this diagnosis. Alternatively, diffuse B-lines in a patchy distribution can be seen in acute respiratory distress syndrome (ARDS). Indeed, the detection of bilateral B-lines in the appropriate clinical scenario is a component of

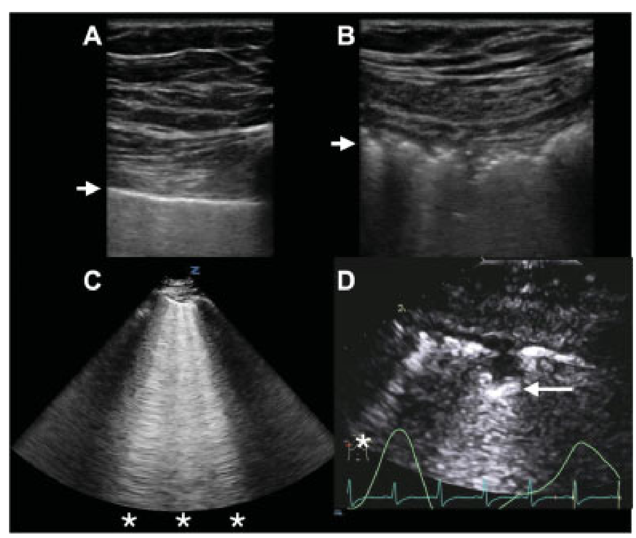

Fig. 3 Lung ultrasound of the pleural line and B-line artifacts. Pulmonary ultrasound exam of the visceral and parietal interface ("pleural line") in patients with showing (**A**) normal pleural line (arrow) with either none or occasional B-lines (**B**) thickened, irregular pleural line (arrow) in a patient with scleroderma and fibrotic lung disease (**C**) multiple B-lines (*) and (**D**) a patient with pneumonia and both a B-line and an irregular subpleural hyperechoic line or "shred sign" (arrow).

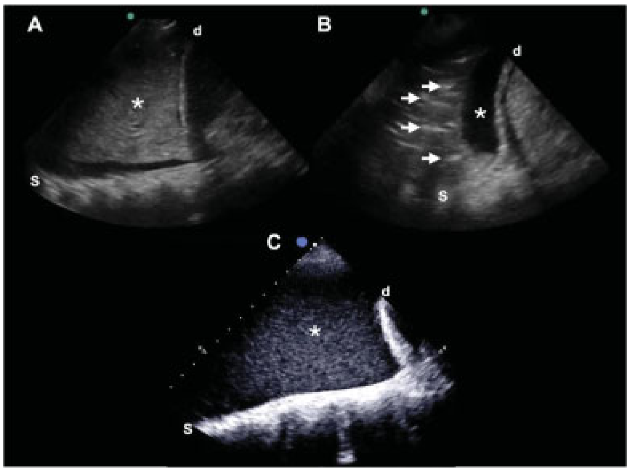

Fig. 4 Bedside ultrasound images of the lung parenchyma and pleural space: (**A**) consolidated or "hepatization" of lung (*), (**B**) static air bronchograms (arrows) with hypoechoic pleural fluid (*), (**C**) homogeneous hyperechoic pleural fluid (*) in a patient with an empyema. d = diaphragm; s = spine shadow.

the Kigali modification of the Berlin definition for ARDS, a proposed means of diagnosing ARDS in resource-limited settings.[25]

Dense, consolidated lung parenchyma that abuts the pleura can be well seen with ultrasound and demonstrates an echogenicity similar to that of the liver, the so-called hepatization (►**Fig. 4A**). The finding of static air bronchograms, hyperechoic short lines or "flecks" within consolidated lung, can be seen in both atelectasis and pneumonia (►**Fig. 4B**). In contrast, dynamic air bronchograms appear as hyperechoic flecks or bubbles within bronchi, move with respiration, and are thought to be highly suggestive of pneumonia (►**Video 1**).[26,27] Meta-analysis of 12 studies containing 1,515 patients showed that LUS is both sensitive (88%) and specific (86%) for detecting pneumonia when compared with chest radiography or chest CT.[28] A contemporary study of patients with acute respiratory failure found that a 9-point lobe-specific pulmonary ultrasound exam was more sensitive than CXR for the identification of lung pathology associated with pneumonia, including interstitial processes (86.2 vs. 28.6%, $p < 0.001$) and ground-glass infiltrates (89.9 vs. 72.5%, $p < 0.001$) when compared with chest CT.[29]

Video 1

Dynamic air bronchograms. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0041-1733896.

LUS is more sensitive than CXR for the detection of pleural effusions.[30,31] In addition, the sonographic pattern of pleural fluid and the pleural space can be helpful in predicting whether a patient has an empyema (►**Fig. 4B, C**). Analysis of 118 thoracenteses performed on 94 critically ill patients with fever and a pleural effusion identified 15 cases of an empyema.[32] There were no empyemas identified among the 83 pleural effusions that demonstrated either an anechoic or relatively homogeneous "nonhyperechoic" fluid pattern. In contrast, all 15 identified empyemas were found among the 35 thoracenteses performed on fluid that had a more complicated, heterogeneous sonographic appearance.

Renal and Bladder Assessment

Overall, POCUS has limited value in diagnosing an infection of the urinary tract system. However, there are several circumstances involving the genitourinary tract in which POCUS can be extremely helpful, including cases of complicated pyelonephritis, infections due to bladder outlet obstruction, or secondary to malfunctioning urinary catheters —all of which can be present in a patient presenting with sepsis. In a retrospective study of 243 patients who presented to an emergency department with acute pyelonephritis, 70% of patients were found to have structural abnormalities on bedside ultrasound exam and these findings contributed to the decision to have 34% of patients undergo a surgical intervention.[33] While many of the reported findings, including nephrolithiasis, can be challenging to identify with POCUS, detecting hydronephrosis can be mastered by bedside practitioners (►**Fig. 5A, B**). In a study involving a variety of emergency medicine clinicians, including attending physicians, medical residents, physician assistants, and medical students, POCUS was moderately sensitive (72.6%) for the detection of hydronephrosis, but improved to 92.7% when performed by attending physicians with advanced ultrasound training.[34] When hydronephrosis is identified by POCUS in a patient with sepsis, an infection of the genitourinary tract must be considered, and it is important that both kidneys and the bladder be evaluated. While bladder outlet obstruction classically presents with bilateral

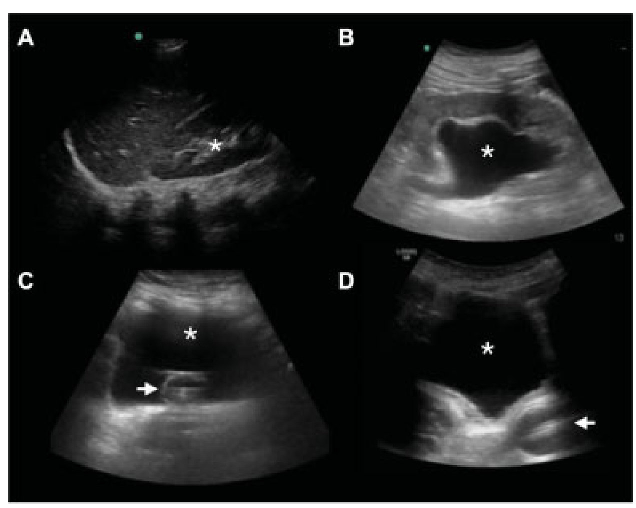

Fig. 5 Renal and bladder ultrasound. (**A**) Normal kidney with hyperechoic renal sinus (*). (**B**) Hydronephrosis with hypoechoic fluid in dilated renal sinus (*). (**C**) Malfunctioning urinary catheter (arrow) in distended bladder (*). (**D**) distended bladder (*) with urinary catheter balloon in vagina (arrow).

hydronephrosis, unilateral hydronephrosis can be seen early in the disease course. A malfunctioning urinary catheter can also be the cause of sepsis. When a urinary catheter is functioning properly, POCUS will reveal a decompressed bladder, but if a urinary catheter balloon is visualized in a distended bladder then urinary catheter malfunction as a cause of sepsis must be considered (►**Fig. 5C**). Bladder ultrasound should also be performed in any patient who has suspected septic shock and is reported to have concomitant oliguria or anuria. If the patient has a urinary catheter and a distended bladder is identified by POCUS, then either a malfunctioning or misplaced urinary catheter must be suspected (►**Fig. 5C, D**). If a distended bladder is noted and the patient does not have a urinary catheter, then urinary retention or bladder outlet obstruction may be present.

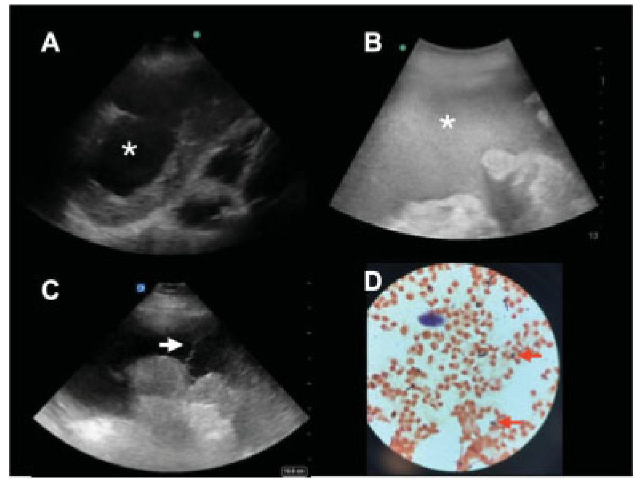

Fig. 6 Abdominal ultrasound: (**A**) liver abscess (*), (**B**) hyperechoic ascites (*) in patient with hemoperitoneum, (**C**) complicated ascites with septations (*), and (**D**) subsequent microscopy of ascites fluid showing budding yeast (arrows) consistent with Candida peritonitis.

Assessment of the Gastrointestinal System

In patients with suspected sepsis, POCUS can be useful in identifying a variety of infectious, or possibly infectious, pathologies involving the gastrointestinal system; these include cholecystitis, bowel perforation, appendicitis, liver abscess, and ascites. The presence of gallstones is central in diagnosing acute cholecystitis, as most patients with cholecystitis have cholelithiasis. Based on a meta-analysis of eight studies ($n = 710$ patients), the sensitivity and specificity of POCUS for the detection of gallstones are 89.8 and 88%, respectively.[35] Perhaps even more importantly, the absence of gallstones on bedside ultrasound exam performed by emergency medicine physicians has been shown to effectively rule out cholecystitis in almost all cases (negative predictive value: 100%, 95% confidence interval [CI]: 85.7–100).[36] Bedside ultrasound techniques for identifying pneumoperitoneum (largely based on an enhanced peritoneal stripe sign) and appendicitis (best described in the pediatric POCUS literature) are described in the emergency medicine literature, but these sonographic findings can be subtle and as a result, these skill sets are largely limited to advanced bedside ultrasound practitioners.[37,38] The identification of a liver abscess by POCUS, albeit its rare, has also been reported (►**Fig. 6A**).[39] Ultrasound is highly sensitive for the identification of intra-abdominal fluid and is capable of detecting volumes as small as 100 mL.[40,41] Whether this fluid is infected and cannot be definitively diagnosed with ultrasound, although there are sonographic clues, which when present, raises the possibility of infection (►**Fig. 6B–D**). Transudative fluid is usually anechoic; on the other hand, exudative abdominal fluid, which can be due to inflammation, hemorrhage, or malignancy, can often appear hyperechoic and contain visible particulates, or septations.[42,43]

Soft-Tissue Assessment

Accurately diagnosing soft-tissue infections based on physical exam findings can be challenging. Both abscesses and necrotizing fasciitis are potential causes of sepsis and must be differentiated from more benign skin and soft-tissue infections such as cellulitis. Cellulitis most commonly presents with "cobblestoning" on ultrasound exam, which is the result of hypoechoic fluid surrounding fat in subcutaneous tissue. It must be noted that the cobblestone finding is not exclusive to cellulitis, as other causes of tissue edema including heart failure and venous insufficiency can also present similarly.[44] And while an abscess frequently occurs in the setting of cellulitis, an ultrasound exam will demonstrate a hypoechoic cavity that is either round or notable for irregular borders. A meta-analysis including 800 patients showed that POCUS is more accurate than clinical examination alone for diagnosing an abscess with an estimated sensitivity and specificity of 97 and 83%, respectively.[45] While ultrasound imaging characteristics of necrotizing fasciitis have been described, no form of imaging, including MRI, can definitively rule out this life-threatening condition or supplant the role of urgent surgical exploration.[46]

Comprehensive Diagnostic Bedside Ultrasound Protocols and Sepsis

To date there are no specific ultrasound protocols for systematically evaluating a patient for sepsis; nonetheless, elements of established POCUS exams for other critically ill patient populations can be applied to patients with possible sepsis. For patients who have suffered blunt trauma, the Focused Assessment with Sonography in Trauma (FAST) and the extended FAST (EFAST) exams have been shown to aid in identifying patients with internal bleeding and guide triage decisions.[47] Both the FAST and EFAST exams include assessing whether there is fluid (presumably blood, in the case of a trauma patient) in the thoracic or peritoneal cavities. In patients with potential sepsis, identification of fluid in these spaces could represent a source of infection. While there are no specific ultrasound strategies for diagnosing septic shock, multiple POCUS protocols have been developed to identify and differentiate patients as having one of four states of shock of Weil and Shubin: hypovolemic, cardiogenic, obstructive, or distributive shock.[9,48] While differences exist, these protocols share many of the same elements (►**Table 1**). Application of the RUSH protocol, for example, could aid in determining whether a patient has features of distributive or cardiogenic shock either of which could be due to sepsis.

POCUS and the Management of Sepsis, Septic Shock, and Source of Infection

Effective source control of infection and timely and appropriate resuscitation are established tenants for the management of sepsis and septic shock.[5] POCUS has been shown to improve the safety of bedside procedures and to aid in resuscitation decisions and its use is associated with improved clinical outcomes in patients with shock.

Bedside Ultrasound and Fluid Responsiveness

After initial fluid resuscitation, approximately 50% of septic patients who remain hypotensive will be fluid responsive, meaning a 500-mL bolus of crystalloid will increase cardiac output of a patient by more than 10%.[49,50] Identifying which patients will be fluid responsive is not straightforward and guessing wrong can be detrimental, as recent resuscitation studies suggest that liberal fluid resuscitation may increase mortality.[51,52] The physiology of fluid responsiveness is based on the relationship between cardiac preload, contractility, and stroke volume. This physiology is defined by the Frank-Starling mechanism, which illustrates how changes in preload affect stroke volume along a curve defined by cardiac contractility. Ultrasound is a valuable tool for the assessment of fluid responsiveness because it allows dynamic evaluation of the components of the Frank-Starling mechanism (preload, cardiac contractility, and stroke volume) and thus improves the clinical prediction of fluid responsiveness.

The simplest ultrasound-guided measure of fluid responsiveness is the assessment of the IVC. The size and collapsibility of the IVC with respiration correlates with right atrial pressure and cardiac preload. In general, an IVC with a diameter of less than 2.1 cm that collapses more than 50% with inspiratory sniff suggests normal central venous pressure and an IVC greater than 2.1 cm with less than 50% collapse is associated with elevated central venous pressure.[53] In patients who were mechanically ventilated without spontaneous respiratory efforts, a mean respirophasic change in IVC diameter of $\geq$15% demonstrated reasonable sensitivity (77%) and specificity (85%) for fluid responsiveness. In contrast, with spontaneously breathing patients, IVC collapsibility as a marker for fluid responsiveness should be used with caution, as studies have shown that enhanced respirophasic change in diameter of $\geq$ 42% has variable sensitivity (30–70%) with reasonable specificity of 80 to 97%.[49,54]

Ultrasound facilitated analysis of dynamic changes in stroke volume and therefore cardiac output offers more direct assessment of fluid responsiveness. For example, positive augmentation of stroke volume caused by an endogenous fluid bolus mediated through a passive leg raise maneuver has been extensively studied and shown to be the most accurate of ultrasound-based tests for predicting fluid responsiveness (sensitivity: 88–92%, specificity: 88–92%) in both spontaneous and mechanically ventilated patients.[49,54] In passively ventilated patients, receiving at least 8 mL/kg of tidal volume, detection of enhanced respirophasic aortic flow variation using Doppler ultrasound has good sensitivity (79%) and specificity (84%) for fluid responsiveness.[49,54] However, this method of monitoring stroke volume variation does not demonstrate the same predictive accuracy in spontaneously breathing patients, or those with arrhythmias or significant right ventricular dysfunction.

Serial Assessment of Resuscitation of the Septic Patient

One of the advantages of bedside ultrasound, as opposed to formal echocardiography, is that it enables serial clinical assessments during the resuscitation and stabilization of critically ill patients. For example, the clinician can easily transition from use of a passive leg-raise maneuver for fluid responsiveness when the patient is spontaneously breathing, to stroke volume variation monitoring assessment after endotracheal intubation. In addition, integration of LUS, in combination with ultrasound-based fluid responsive studies, can add nuance to resuscitation management. The sudden development of B-lines in a patient with previously normal lung sonography indicates the development of interstitial edema and should prompt a rapid transition from fluid administration to vasoactive medications for hemodynamic stabilization. In the setting of anuria or oliguria despite fluid or vasoactive therapy, it is useful to perform a bedside bladder ultrasound confirm that urine output is being accurately measured. A simplistic bladder scanner does not permit direct visualization of the pelvis and cannot always differentiate urine within a bladder from other fluids that may be in the pelvis including ascites.[55] Moreover, suboptimal urine output in a patient with suspected sepsis may be a function of either a malfunctioning urinary catheter or a urinary catheter which is improperly positioned outside of the bladder (►**Fig. 5D**).

Bedside Ultrasound to Assist in Diagnostic Procedures and Infectious Source Control

Ultrasound guidance has become the standard for many bedside procedures that are integral in the management of septic patients. "Static" ultrasound imaging (when ultrasound is solely used to identify the site for needle entry, but the procedure itself is performed without ultrasound guidance) for thoracentesis has been shown to be superior to the landmark-based technique in terms of both safety and diagnostic yield.[56] More recently, a retrospective study (single center, 394 total patients) showed that "real-time" ultrasound guidance (when the needle advancement is visualized with ultrasound imaging) significantly reduced the incidence of pneumothoraces associated with thoracentesis procedures ($p = 0.02$) and reduced the total number of pneumothorax complications with thoracostomy tube placement, although not statistically significant ($p = 0.4$).[57] Likewise, paracentesis, the standard of care for a patient with ascites and suspected sepsis, has been shown to be more successful if real-time ultrasound guidance, as opposed to traditional landmark approach, is performed (►**Video 2**).[58]

Video 2

Real-time ultrasound-guided paracentesis. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0041-1733896.

Ultrasound guidance is also likely beneficial in the management of soft-tissue abscesses. In a retrospective study of 377 pediatric patients with suspected skin abscesses, treatment failure rates (defined as need for incision or drainage after the initial emergency department visit) were significantly lower in cases in which evaluation included a bedside ultrasound exam (4.4 vs. 15.6%, $p < 0.005$).[59] Lumbar puncture, necessary to both diagnose meningitis and identify the causative organism, has also been shown to be more successfully performed when ultrasound guidance is employed.[60] Meta-analysis of 320 patients (a subset of a much larger study) undergoing lumbar puncture showed that ultrasound significantly reduced the risk of a failed procedure (risk reduction = 0.19 [CI: 0.07–0.56]) with a number needed to treat of 9.

Conclusion

Patients with suspected sepsis or septic shock present distinct challenges to the bedside clinician. Optimal clinical care requires a timely and accurate diagnosis, source control, and, in cases of shock, appropriate resuscitation. POCUS has been shown to aid in all these aspects of sepsis clinical care. But for bedside ultrasound to be most effective, a multisystem approach should be taken. Just as a conscientious clinician performs a complete physical exam, a bedside ultrasound exam to evaluate a patient with suspected sepsis should not be limited to a subset of organ systems. Instead, information gathered from an integrated, comprehensive bedside ultrasound exam should be combined with careful history-taking, a traditional physical exam, and laboratory studies to create a more thorough clinical assessment of the patient. If a potential source of infection is identified, then POCUS may be used to improve both the success and safety of a variety of bedside drainage procedures. Furthermore, in the event the patient has septic shock, serial bedside ultrasound exams should be employed to titrate and personalize resuscitative efforts. Ultimately, those who advocate for the expanded use of bedside ultrasound are not suggesting that traditional clinical approaches be abandoned. POCUS will never replace the stethoscope or the need for a formal echocardiogram. Rather, bedside ultrasound should be viewed as a powerful complementary tool which can be used at multiple stages in the diagnosis and treatment of patients with sepsis and septic shock.

Conflict of Interest
None declared.

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