Received: 20 December 2019 | Revised: 22 January 2020 | Accepted: 23 January 2020

DOI: 10.1002/emp2.12028

JACEP OPEN
JOURNAL OF THE AMERICAN COLLEGE OF EMERGENCY PHYSICIANS OPEN
A GLOBAL JOURNAL OF EMERGENCY MEDICINE
Open Access

WILEY

CONCEPTS

Imaging

Clinical ultrasonography in patients who inject drugs (the CUPID protocol): an illustrated case series

Stephanie C. DeMasi MD | Laura E. Goyack MD | Erin F. Shufflebarger MD | Erik P. Hess MD, MSc | Rachel M. Skains MD | Maxwell A. Thompson MD | Samuel Luke Burleson MD | John P. Gullett MD | David C. Pigott MD

Department of Emergency Medicine, University of Alabama at Birmingham, Birmingham, Alabama

Correspondence
David C. Pigott, MD, FACEP, 619 S 19th St., OHB 251, Department of Emergency Medicine, The University of Alabama at Birmingham, Birmingham, AL 35249-7013, USA.
Email: dpigott@uabmc.edu

Funding and support: By *JACEP Open* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

Abstract

In 2017, there were ≈47,600 opioid overdose-related deaths in the United States. US emergency department (ED) visits for suspected opioid overdose increased by 30% between July 2016 and September 2017.[2] The current US opioid epidemic makes it critical for emergency physicians to be aware of common and uncommon infectious and non-infectious complications of injection drug use. Point-of-care ultrasound has become a widely available, non-invasive diagnostic tool in EDs across the United States and worldwide. The increasing population of injection drug use patients is at risk for serious morbidity and mortality from an array of disease states amenable to ultrasound-based diagnosis. We propose a protocol for clinical ultrasonography in patients who inject drugs (the CUPID protocol), a focused, 3-system point-of-care ultrasound approach emphasizing cardiovascular, thoracic, and musculoskeletal imaging. The protocol is a screening tool, designed to detect high risk infectious and noninfectious complications of injection drug use.

KEYWORDS

emergency medicine, infection, opioid-related disorders, substance abuse—intravenous, ultrasonography

1 | INTRODUCTION

In 2017, there were ≈47,600 opioid overdose-related deaths in the United States, with the rate of synthetic opioid drug overdose deaths (other than methadone) nearly tripling between 2015 and 2017, an increase largely because of illicitly manufactured fentanyl.[1-3] The prevalence of opioid use and opioid-related complications continues to increase. In 2016, over 183,000 US emergency department (ED) visits occurred because of unintentional opioid toxicity.[3] US ED visits for suspected opioid overdose increased by 30% between July 2016 and September 2017.[1,4] Well-known complications of injection drug use include blood-borne infections such as HIV and hepatitis B and C, infective endocarditis, pulmonary infections, vascular injuries, and soft tissue infections. Less common complications include pneumothorax, hemothorax, empyema, and complications related to infective endocarditis, such as infectious intracranial aneurysms, septic emboli, glomerulonephritis, and embolic splenic and renal infarction.[5]

A comprehensive diagnostic approach is typically recommended to evaluate the injection drug use patient because injection drug use subjects them to multiple risk factors for common and uncommon

Supervising editor: Steven G. Rothrock, MD.

infections. These risk factors include sharing of used or dirty needles, unhygienic practices, and immunocompromised states (including HIV and hepatitis C). Although this approach is generally guided by the presenting complaint and physical examination findings, injection drug use patients are at increased risk for infection and other serious complications that may not be readily apparent.[5] The presence of occult infections and other sequelae of injection drug use can be evaluated through a focused, multi-system approach using ultrasonography. An additional benefit of such an approach stems from early diagnosis, permitting rapid initiation of appropriate therapy. Point-of-care ultrasound has become a widely available non-invasive diagnostic tool in emergency departments across the United States and worldwide. We propose a rapid, 3-system, point-of-care ultrasound-based approach to evaluate the injection drug use patient designed not only to diagnose injection drug use complications, but also to expedite patient care, because point-of-care ultrasound may provide definitive diagnoses that obviate the need for further diagnostic imaging. The ability of point-of-care ultrasound to direct patient management decisions nearly simultaneously with the patient's initial evaluation lends further support to this approach.

2 | PROTOCOL DESCRIPTION

This article proposes a simple, 3-system point-of-care ultrasound protocol that integrates existing ultrasound imaging guidelines with a clinical approach to the evaluation of the injection drug use population that emphasizes the early identification of serious complications. The authors have named this approach the CUPID protocol (clinical ultrasonography in patients who inject drugs). The three anatomic systems evaluated by the protocol are cardiovascular, thoracic, and musculoskeletal. Each portion of the exam is designed to detect high-risk injection drug use complications based on the point-of-care ultrasound evaluation of specific anatomic regions.

Who needs the CUPID protocol? Injection drug use patients with a clinical presentation concerning for infectious or non-infectious complications of injection drug use may benefit from the CUPID protocol. Although we suggest the thoracic and cardiovascular exams be performed together, the musculoskeletal portion may be confined to patients presenting with extremity-related complaints. Although not every ED patient who injects drugs necessarily requires all portions of the CUPID protocol, the ease of implementation of this 3-step approach may lead to early diagnosis of high-risk infectious processes as well as decreased use of other imaging modalities.

The CUPID protocol is performed using a standard ultrasound system with commonly available transducers. A phased-array transducer (3.5–5 MHz) is recommended for cardiac and thoracic imaging and a linear array transducer (7.5–10 MHz) for musculoskeletal and vascular evaluations. Deeper musculoskeletal structures, such as the hip joint, may be better imaged with a curvilinear transducer (2–5 MHz). A video tutorial is available that illustrates the performance of the CUPID protocol (see Video S1). Below, we have provided the clinical rationale and a detailed description of the technique, categorized by anatomic area.

2.1 | Cardiovascular

The cardiovascular portion of the CUPID protocol emphasizes the detection of valvular pathology, including valvular vegetations consistent with infective endocarditis, regurgitation from current or previous infective endocarditis, and right heart strain, a common complication of tricuspid valvular failure. Less common cardiac pathology in this patient population may also be seen, including pericardial effusions or the presence of impaired left ventricular function. Other vascular injuries related to injection drug use that are amenable to detection using point-of-care ultrasound include pseudoaneurysm formation because of inadvertent arterial injection, hematoma, or intravascular foreign body.

Standard echocardiographic views should be obtained, if possible, including parasternal long and short axis, apical 4-chamber, subxiphoid, and inferior vena cava (IVC). Because of the clinical concern for infective endocarditis in injection drug use patients, color Doppler should be incorporated into this portion of the CUPID protocol to evaluate for the presence of valvular regurgitation, stenosis, or flail leaflet. Ensure that color Doppler settings are optimized to detect regurgitation by using a small color sector box at the appropriate depth and velocity scale. For most ultrasound systems, the pulse repetition factor or velocity scale is set automatically.[6] The apical four-chamber view provides a useful echocardiographic window for visualizing valvular vegetations as well as assessing for the presence of regurgitation. The absence of visible vegetations does not exclude infective endocarditis, because the detection rate for vegetations by transthoracic echocardiography is relatively low (~60%).[7] Peripheral vascular injuries such as pseudoaneurysm, hematoma, or intravascular foreign body are best detected using a high frequency linear array transducer. Color Doppler or power Doppler modes may be used to further evaluate suspected vascular injury.

2.2 | Thoracic

The thoracic portion of the CUPID protocol is designed for a rapid evaluation of the dyspneic injection drug use patient. Although the ED evaluation of the stable injection drug use patient with mild respiratory symptoms is unlikely to differ from that of the non-injection drug use patient, the injection drug use patient with more severe respiratory symptoms is an excellent point-of-care ultrasound candidate. The thoracic portion of the CUPID protocol may detect pneumonia, pleural effusion, empyema, pneumothorax, or non-cardiogenic pulmonary edema, a rare but potentially lethal complication of opioid use.[8] As noted in Table 1, pneumonia is disproportionately present in the injection drug use population, an ≈10-fold risk over the general population.[9]

The thoracic views should include standard point-of-care ultrasound evaluation of the chest wall, lungs, and pleural space. The well-validated BLUE protocol provides an excellent framework for ultrasound evaluation of the thorax, specifying the detection of artifacts ("A lines" and "B lines"), lung sliding, and the presence of alveolar consolidation and/or pleural effusion.[10,11] It should be noted, however, that the

TABLE 1 Comparison of infectious disease prevalence among ED patients and as a percentage of hospital admissions, injection drug use versus all patients

Disease	Prevalence in ED patients with injection drug use (%)	Prevalence among all ED patients (%)
HIV	7.5–9[29,30]	0.8–5.6[31,32]
Hepatitis C	38–47[33,34]	14[35]
MRSA bacteremia	4.9[36]	1.4[36]
	% of hospital admissions, injection drug use	**% of hospital admissions, all patients**
Infective endocarditis	3.8[37]	0.1[38]
Skin and soft tissue infections	18.2[37]	1.8[39]
Pneumonia	26.7[37]	2.5[40]
Septic arthritis	2.6[37]	0.31[41]

TABLE 2 Description and clinical course of ED injection drug use patients with infectious complications

Age	Sex	Chief complaint	ED imaging	Time to point-of-care ultrasound (min)	Time to final imaging report (min)	Diagnosis	Disposition
27	Female	Chest pain, dyspnea, fever	Point-of-care ultrasound Chest x-ray Chest CT	9	211	Pneumonia, empyema	Admit
28	Male	Productive cough, dyspnea, fatigue	Point-of-care ultrasound Chest x-ray	6	1138	Infective endocarditis	ICU
29	Male	Possible needle in groin	Point-of-care ultrasound	17	NA	Intravascular needle fragment	Admit
46	Male	Right hip pain	Point-of-care ultrasound Hip x-ray Pelvis CT	91	240	Septic arthritis	OR

BLUE protocol has not been validated for use in patients without acute dyspnea. In the injection drug use patient, the thoracic and cardiovascular components of the CUPID protocol should generally be performed together, because coexisting cardiopulmonary complications of injection drug use may be otherwise overlooked.

2.3 | Musculoskeletal

The musculoskeletal portion of the CUPID protocol is intended to detect infections and injuries to superficial and deep musculoskeletal structures, including cellulitis, abscess, and septic arthritis. Although the presence of cellulitis may be evident on clinical examination, multiple studies have confirmed that clinical examination alone is inferior to point-of-care ultrasound for the detection of underlying abscess, with point-of-care ultrasound changing management in 17%–56% of adult patients.[12,13] Joint effusion or septic arthritis may also be detected using point-of-care ultrasound, expediting operative intervention.[14] The presence of subcutaneous gas is also readily apparent on point-of-care ultrasound exam and is suggestive of necrotizing soft tissue infection, a condition requiring emergent surgical intervention for definitive management. As noted in the accompanying Table 1, injection drug use patients are at markedly increased risk for skin and soft tissue infections as well as septic arthritis.

The musculoskeletal component of the CUPID protocol should be adapted to the injection drug use patient's presenting complaint. A painful extremity or joint, areas of focal swelling or tenderness, or clinical suspicion for underlying infection should all be considered indications for a directed, point-of-care ultrasound-based musculoskeletal assessment. Patients with less common injection drug use complications, such as a suspected soft tissue foreign body or subcutaneous gas, may also benefit from point-of-care ultrasound evaluation, potentially resulting in significant changes in management.

The following illustrated case series highlights important examples of the use of the CUPID protocol in the ED evaluation of the injection drug use patient. Point-of-care ultrasound images are accompanied by a brief patient presentation and summary of the patient's clinical course. All ultrasound examinations were performed by emergency medicine residents with supervising emergency physicians during the patients' initial ED evaluation. Table 2 summarizes the demographics and clinical course for the 4 patients described here and also highlights the markedly reduced time to diagnosis associated with point-of-care ultrasound versus computed tomography (CT) imaging or comprehensive echocardiography. The cases are categorized by each of the three anatomic systems evaluated by the CUPID protocol: cardiovascular, thoracic and musculoskeletal, as seen in the accompanying diagram (Figure 1).

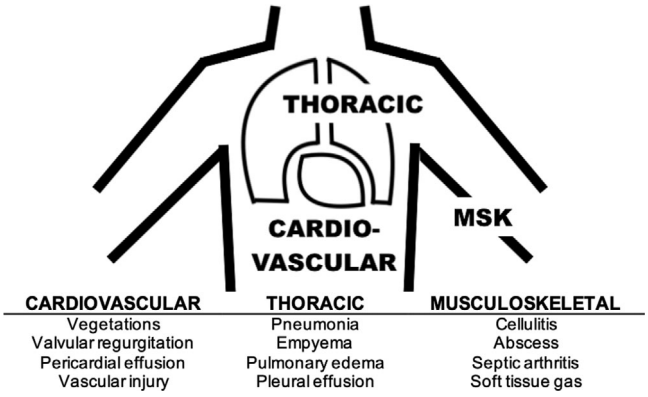

FIGURE 1 Anatomic systems evaluated by CUPID protocol

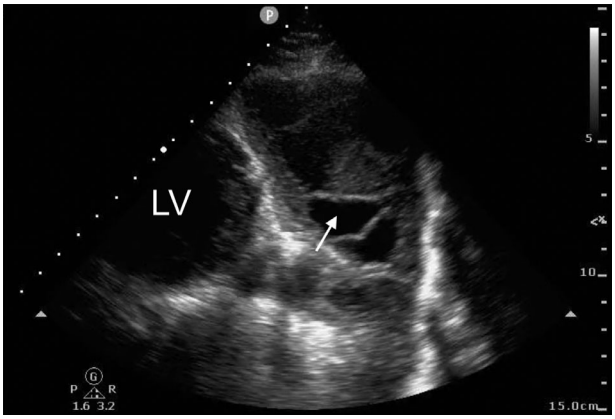

FIGURE 2 Transthoracic ultrasound view demonstrating a complex, loculated left pleural effusion with echogenic rind concerning for empyema (arrow). A short axis view of the left ventricle (LV) is also seen to the left of the image

3 | CUPID PROTOCOL CASES

3.1 | Case 1—cardiovascular and thoracic

A 27-year-old female with history of injection drug use and hepatitis C presented to the ED for chest pain, dyspnea, and fever. The patient stated that she had been febrile and dyspneic with constant left-sided chest pain for the past 5 days. The patient admitted to regular intravenous heroin and methamphetamine use. Initial vital signs were blood pressure 118/64 mm Hg, pulse rate 145 beats/minute, respiratory rate 22 breaths/minute, temperature 100.9°F (38.2°C), and oxygen saturation 97% on room air. On examination, she was anxious and in moderate distress. Pulmonary examination was significant for tachypnea with left-sided crackles and coarse breath sounds. Skin exam was notable for linear needle marks in the bilateral antecubital fossae. There was no appreciable cardiac murmur. Laboratory evaluation was remarkable for a leukocytosis of 12,850/mm^3. EKG showed sinus tachycardia. Point-of-care ultrasound of the thorax demonstrated a complex left-sided heterogeneous pleural fluid collection with multiple fibrin septations and an echogenic peripheral rind suggestive of empyema (Figure 2).

There were no valvular vegetations seen on limited bedside transthoracic echocardiogram. Chest radiograph demonstrated a large dense opacity in the left mid and lower lung zones. Contrast-enhanced chest computed tomography (CT) revealed a loculated left pleural effusion/empyema with near complete left lower lobe atelectasis.

The patient was resuscitated with intravenous fluids and started on broad-spectrum antibiotics including vancomycin to cover for methicillin-resistant *Staphylococcus aureus* (MRSA) given her injection drug use history. A 14 French chest tube was placed in the left thorax with minimal output. The patient was admitted with plans to undergo video-assisted thoracoscopic surgery for her empyema, which she later declined. Blood and pleural fluid cultures were positive for MRSA, leading to a final diagnosis of MRSA pneumonia and empyema. Incidentally, the patient also tested positive for tuberculosis and was started on a multi-drug outpatient regimen.

3.2 | Case 2—cardiovascular and thoracic

A 28-year-old male with a history of injection drug use and bipolar disorder presented with a 2-week history of cough productive of brown sputum, fatigue, and dyspnea. The patient also endorsed weight loss and dark maroon spots to his feet and ankles that he noticed 2 days before arrival. Initial vital signs were blood pressure 95/53 mmHg, pulse rate 122 beats/minute, respiratory rate 21 breaths/minute, oxygen saturation 99% on room air. During his ED course, the patient became febrile to 101°F (38.4°C). Physical examination was notable for bilateral lower extremity edema with diffuse petechiae and purpura. Breath sounds were coarse with crackles bilaterally. A systolic murmur was noted. He was also found to have needle marks in the left antecubital fossa.

Laboratory evaluation was notable for a lactic acid of 2.5 mmol/L and a white blood cell count of 17,210/mm^3. The patient was also found to be thrombocytopenic with a platelet count of 17,100/mm^3. Troponin I was also elevated at 0.045 ng/mL. Hepatitis C antibody was positive. Point-of-care ultrasound was notable for a large (>3 cm) mobile vegetation on the tricuspid valve, moderate tricuspid regurgitation, a small pericardial effusion, and a right pleural effusion (Figure 3). Further imaging with a non-contrast chest CT showed evidence of multiple septic emboli and pulmonary infarctions.

The patient was resuscitated with intravenous fluids, started on broad-spectrum antibiotics, and admitted to the intensive care unit. Blood cultures obtained in the ED were positive for methicillin-sensitive *Staphylococcus aureus* (MSSA). His clinical course was complicated by acute kidney injury requiring hemodialysis, multiple blood transfusions, and thoracentesis for bilateral pleural effusions.

3.3 | Case 3—musculoskeletal and cardiovascular

A 29-year-old male with a history of injection drug use and hepatitis C arrived by emergency medical services (EMS) following an intravenous

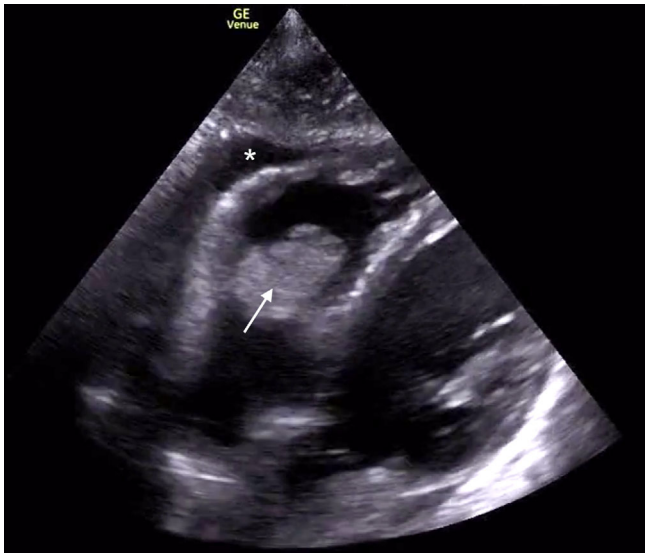

FIGURE 3 Subxiphoid cardiac ultrasound view demonstrating a large (>3 cm) vegetation (arrow) adherent to the tricuspid valve consistent with infective endocarditis. A pericardial effusion is also present (asterisk)

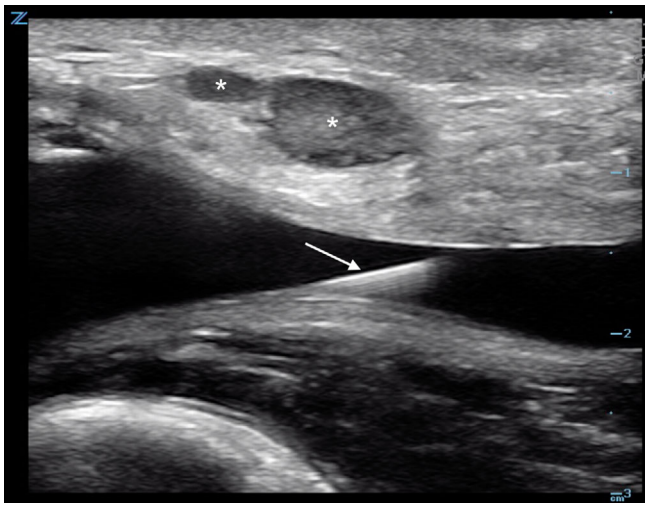

FIGURE 4 Longitudinal ultrasound view of the right inguinal region demonstrating an echogenic linear foreign body (arrow) with prominent "ring-down" artifact within the right common femoral vein. Small inguinal lymph nodes are incidentally noted superficial to the vessel (asterisks)

drug overdose. EMS administered 2 mg intravenous naloxone before ED arrival with good response. On arrival, the patient stated that he thought a needle "broke off" while he was injecting heroin and methamphetamine into his left groin earlier that day and complained of pain at the site. Initial vital signs were within normal limits. On examination, he was drowsy but easily arousable. The patient's femoral pulses were equal and symmetric. There was no visible or palpable foreign body in the left groin. Skin examination revealed mild erythema of the left lower extremity from the ankle to the thigh. Laboratory evaluation was remarkable for leukocytosis of 13,700/mm^3. Point-of-care ultrasound was used to further evaluate the area, given the concern for possible retained foreign body following presumed femoral venipuncture. Ultrasound was performed using a high-frequency linear array transducer and revealed an echogenic linear foreign body within the left common femoral vein with prominent "ring-down" artifact consistent with an intravascular needle fragment (Figure 4).

The patient underwent successful fluoroscopically guided foreign body removal by interventional radiology, yielding a broken needle fragment consistent with the patient's history. The patient was admitted to the hospital on intravenous vancomycin and piperacillin/tazobactam for left lower extremity cellulitis. He was discharged in good condition 3 days later on a course of oral cephalexin.

3.4 | Case 4—musculoskeletal

A 46-year-old male with a history of injection drug use currently on methadone presented to the ED with several days of severe right hip pain and inability to ambulate. The patient denied a history of fever, chills, or trauma to the affected extremity. He had a prior history of injection drug use but reported his last use was >5 years prior to

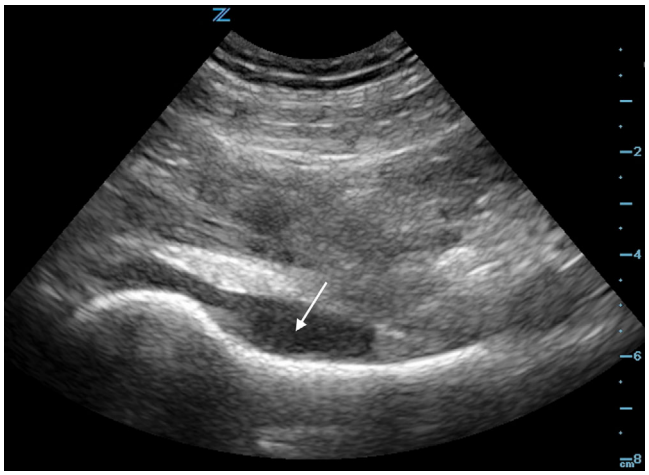

FIGURE 5 Longitudinal ultrasound view of the right proximal femur demonstrating a hypoechoic fluid collection anterior to the femoral head and neck (arrow)

presentation. The patient was afebrile with normal vital signs. Physical examination was notable for severe pain with passive internal and external rotation of the right hip. He was unable to bear weight on the right lower extremity.

Laboratory evaluation was notable for elevated C-reactive protein of 167 mg/L, elevated erythrocyte sedimentation rate at 46 mm/hour, and normal leukocyte count of 4900/mm^3. Plain radiographs of the right hip were obtained and were unremarkable. Point-of-care ultrasound of the right hip demonstrated a right hip effusion surrounding the femoral neck (Figure 5). Further imaging with non-contrast CT of the pelvis showed a small rim-enhancing right hip joint collection.

The patient subsequently underwent ultrasound-guided aspiration of the right hip effusion. Approximately 20 mL of purulent synovial fluid

was aspirated, with a fluid leukocytosis of 32,335/mm^3 and 0 red blood cells. The patient was taken promptly to the operating room by orthopedic surgery for irrigation and debridement of the right hip. Joint cultures obtained intraoperatively were positive for *Serratia marcescens*. Following the procedure, the patient was initially started on broad-spectrum antibiotics, and subsequently completed a 2-month course of oral ciprofloxacin for *Serratia* septic arthritis.

4 | DISCUSSION

This case series demonstrates the use of point-of-care ultrasound in the diagnosis of both common and uncommon complications of injection drug use. The increasing prevalence of injection drug use patients has led to a corresponding rise in the incidence of infectious injection drug use complications and a surge of injection drug use-related ED visits. Data collected from the National Survey of Drug Use and Health indicate that the use of heroin has nearly doubled between 2006 and 2013 and that the proportion of infective endocarditis hospitalizations related to injection drug use has increased concomitantly, from 7%–12.1%.[15,16] Skin and soft tissue infections related to injection drug use are also on the rise and are amenable to ultrasound-aided diagnosis. One study found that hospitalization rates for opiate-related skin and soft tissue infections more than doubled from 4–9/100,000 between 1993 and 2010, with most of the increase occurring among individuals aged 20–40.[17] A prospective cross-sectional study in San Francisco found that ≈32% of active injection drug uses had a drug-related abscess or cellulitis at the time of enrollment.[18] The true incidence of soft tissue infections in this patient population is difficult to estimate, as most are self-treated and likely under-reported. Additionally, injection drug use patients have been found to have a 10-fold increased risk of community-acquired pneumonia compared with the general population.[9] The markedly increased risk for infectious complications of injection drug use is evident in the increased prevalence of blood-borne infections, such as HIV, hepatitis C, and MRSA bacteremia, as well as notably higher rates of common and uncommon infectious diseases such as pneumonia, skin and soft tissue infections, infective endocarditis, and septic arthritis (Table 1).

Point-of-care ultrasound is a widely available, non-invasive, and inexpensive imaging modality. The scope of practice for bedside ultrasound continues to grow with expanding indications and increasing user experience. Common clinical scenarios evaluated by point-of-care ultrasound include the trauma patient using the focused assessment with sonography in trauma (FAST) exam, the hemodynamically unstable patient with the rapid ultrasound for shock and hypotension (RUSH) exam,[19] cardiovascular assessment during cardiac arrest, deep venous thrombosis and evaluation for right heart strain, obstetric evaluation, musculoskeletal evaluation, and the patient with abdominal pain, among others.[20] To date, although there is no standardized ultrasound protocol designed to evaluate the symptomatic injection drug use patient, areas of potential concern in this population overlap with several existing ultrasound protocols. The CUPID protocol was developed to provide a unified, ultrasound-based strategy to simplify and expedite the ED evaluation of the injection drug use patient, emphasizing focused cardiac, thoracic, and musculoskeletal examinations. As illustrated in this case series, point-of-care ultrasound findings enabled clinicians to rapidly obtain a working diagnosis, expediting consultation, and definitive therapy.

In Case 1, the thoracic portion of the CUPID protocol demonstrated an unexpected diagnosis that resulted in a significant change in patient management. There is good evidence that thoracic ultrasound is more sensitive than chest radiography for identifying pleural effusion, approaching the accuracy of chest CT (with reported sensitivities of 39% and 92% for chest radiography and lung ultrasound, respectively, compared to CT).[21] Additionally, sonographic findings can effectively distinguish between a transudative and exudative effusion. Sonographic characteristics of an exudative pleural effusion include the presence of heterogeneous or echogenic fluid with a visible swirling pattern, fibrin septations, or even an echogenic peripheral rind, a finding that has also been associated with empyema.[22] In this case, ultrasound findings suggested empyema rather than a transudative pleural effusion (Figure 2), supporting the decision for chest tube placement by providing information not visible on chest radiography or on CT. Within a few minutes of the patient's arrival, point-of-care ultrasound demonstrated the presence of a complex infectious pulmonary process in an injection drug use patient that would require a concerted, multidisciplinary approach involving multiple medical and surgical subspecialties. Although the patient did receive additional imaging, point-of-care ultrasound provided a working diagnosis within minutes of patient arrival, guiding the patient's further management and providing information not seen on other imaging studies.

Case 2 illustrates the use of the cardiovascular portion of the CUPID protocol in the evaluation for suspected infective endocarditis using limited bedside echocardiography. An initial presentation of bilateral lower extremity purpuric rash, tachycardia, thrombocytopenia, and fever lends itself to a broad differential diagnosis, including meningococcemia, thrombotic thrombocytopenic purpura, idiopathic thrombocytopenic purpura, disseminated intravascular coagulation, hemolytic uremic syndrome, and sepsis, among others. With the benefit of point-of-care ultrasound, the diagnosis of right-sided infective endocarditis was made shortly after arrival, allowing timely initiation of appropriate therapy, as well as the diagnosis of multiple complicating factors, including pericardial and pleural effusions. Because the initial cardiac point-of-care ultrasound provided a conclusive diagnosis, formal echocardiography was not obtained until the next hospital day. Case 3 also used the cardiovascular section of the CUPID protocol, again resulting in a definitive diagnosis shortly after patient arrival. The ultrasound-based diagnosis of an intravascular foreign body, a complication in injection drug use patients associated with significant potential morbidity,[23] permitted a rapid transfer to the interventional radiology suite for prompt removal. Although point-of-care ultrasound was not performed in the patient in Case 4 immediately on arrival, it still provided an expedited diagnosis of septic arthritis in an injection drug use patient hours before hip CT could be performed and interpreted. Invasive infections by *Serratia*, although less

common than other causes of septic arthritis such as *Staphylococcus* or *Streptococcus* species, have been well described as pathogens in the injection drug use population.[24] Point-of-care ultrasound has also been described in the diagnosis of septic arthritis in multiple other anatomic locations.[25] As noted in Table 1, point-of-care ultrasound served to provide a diagnosis within minutes that might have otherwise taken hours and multiple consultations to establish. Although additional diagnostic imaging was obtained in some of these cases, point-of-care ultrasound supplied essential clinical data that guided the remainder of the patient's ED evaluation and management. The use of such diagnostic information early in the patient's ED stay should not be underestimated.

As illustrated in the cases detailed above, the CUPID protocol demonstrates the use of a rapid, focused diagnostic approach to the evaluation of the injection drug use patient for the presence of high-risk infections such as infective endocarditis and empyema as well as less evident complications such as septic arthritis and intravascular foreign body. In each of these cases, point-of-care ultrasound served to expedite diagnosis and appropriate intervention, often within minutes of patient arrival. Emergency physicians and other healthcare providers can use this protocol to streamline their diagnostic approach to a vulnerable patient population that is likely to increase in size during the months and years to come. Similarly, resource-limited settings are also likely to benefit from the use of the CUPID protocol, where injection drug use patient populations may be at even greater risk for morbidity and mortality because of disproportionate levels of HIV or tuberculosis coinfection.[26,27]

The opioid epidemic makes it critical for emergency physicians to be aware of common and uncommon infectious and non-infectious complications in injection drug use patients. Emergency physicians have made significant strides with point-of-care ultrasound and have developed concise, useful algorithms to assist in the rapid evaluation of critically ill and injured ED patients. The ED patient with a history of active injection drug use also represents a high-risk clinical scenario and requires a similar degree of vigilance. Because the trend of increasing opioid-related morbidity and mortality continues unabated—by 2016 the number of opioid-related deaths (>42,000) surpassed even the number of motor vehicle traffic deaths (~39,000)—we strongly recommend enhanced surveillance and caution in the evaluation of injection drug use patients in the ED setting.[3,28]

5 | CONCLUSION

We advocate that point-of-care ultrasound be considered an essential tool in the clinical evaluation of this patient population and propose that the CUPID protocol, with its simple, three-system approach, provides an opportunity for improved diagnosis and expedited treatment of injection drug use patients. Point-of-care ultrasound, as refined by the CUPID protocol for the injection drug use population, is ideally situated as a rapid, accurate method of assessing injection drug use patients for medical or surgical disease. Given its ability to diagnose both localized complications such as soft tissue infections, vascular injury, or septic arthritis as well as systemic illnesses such as infective endocarditis, point-of-care ultrasound facilitates prompt evaluation and management of this vulnerable group. Additional research comparing the prospective implementation of the CUPID protocol versus standard management in ED injection drug use patients may have significant value in determining its future use. Although this protocol has not yet been validated using prospective analysis, we believe the CUPID protocol has the potential to have a positive clinical impact on this growing, susceptible patient population by providing a simple, ultrasound-based strategy for the assessment of patients at risk for the most serious injection drug use complications.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

David C. Pigott MD https://orcid.org/0000-0002-9699-9327

REFERENCES

1. Scholl L, Seth P, Kariisa M, et al. Drug and opioid-involved overdose deaths - United States, 2013–2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(5152):1419-1427.
2. Vivolo-Kantor AM, Seth P, Gladden RM, et al. Vital signs: trends in emergency department visits for suspected opioid overdoses - United States, July 2016-September 2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(9):279-285.
3. Hedegaard H, Minino AM, Warner M. Drug overdose deaths in the United States, 1999–2017. *NCHS Data Brief*. 2018(329):1-8.
4. Centers for Disease Control and Prevention. 2019 Annual Surveillance Report of Drug-Related Risks and Outcomes — United States. In: Surveillance Special Report. Vol 2019: Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. 2019.
5. Grosheider T, Shepherd SM. Injection drug users. In: Tintinalli JE, Stapczynski JS, Ma OJ, Yealy DM, Meckler GD, Cline DM, (Eds.), *Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 8e*. New York, NY: McGraw-Hill Education; 2016.
6. Thomas JD. Doppler echocardiographic assessment of valvar regurgitation. *Heart*. 2002;88(6):651-657.
7. Bai AD, Steinberg M, Showler A, et al. Diagnostic accuracy of transthoracic echocardiography for infective endocarditis findings using transesophageal echocardiography as the reference standard: a meta-analysis. *J Am Soc Echocardiogr*. 2017;30(7):639-646.e638.
8. Radke JB, Owen KP, Sutter ME, et al. The effects of opioids on the lung. *Clin Rev Allergy Immunol*. 2014;46(1):54-64.
9. Hind CR. Pulmonary complications of intravenous drug misuse. 2. Infective and HIV related complications. *Thorax*. 1990;45(12):957-961.
10. Lichtenstein DA, Meziere GA. Relevance of lung ultrasound in the diagnosis of acute respiratory failure: the BLUE protocol. *Chest*. 2008;134(1):117-125.
11. Cremonese RV, Raupp ACT, de Andrade JMS, et al. Validation of a lung ultrasound protocol in acute respiratory failure: preliminary results. *Critical Care*. 2013;17(suppl 2):P147-P147.
12. Subramaniam S, Bober J, Chao J, et al. Point-of-care ultrasound for diagnosis of abscess in skin and soft tissue infections. *Acad Emerg Med*. 2016;23(11):1298-1306.
13. Barbic D, Chenkin J, Cho DD, et al. In patients presenting to the emergency department with skin and soft tissue infections what is the

diagnostic accuracy of point-of-care ultrasonography for the diagnosis of abscess compared to the current standard of care? A systematic review and meta-analysis. *BMJ Open*. 2017;7(1):e013688.
14. Minardi JJ, Lander OM. Septic hip arthritis: diagnosis and arthrocentesis using bedside ultrasound. *J Emerg Med*. 2012;43(2):316-318.
15. Administration SAMHS. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings. NSDUH Series H-48, HHS Publication No. (SMA) 14–4863, 2014. https://www.samhsa.gov/data/sites/default/files/NSDUHresultsPDFWHTML2013/Web/NSDUHresults2013.pdf. Accessed April 10, 2019.
16. Wurcel AG, Anderson JE, Chui KK, et al. Increasing infectious endocarditis admissions among young people who inject drugs. *Open Forum Infect Dis*. 2016;3(3):ofw157.
17. Ciccarone D, Unick GJ, Cohen JK, et al. Nationwide increase in hospitalizations for heroin-related soft tissue infections: associations with structural market conditions. *Drug Alcohol Depend*. 2016;163:126-133.
18. Binswanger IA, Kral AH, Bluthenthal RN, et al. High prevalence of abscesses and cellulitis among community-recruited injection drug users in San Francisco. *Clin Infect Dis*. 2000;30(3):579-581.
19. Perera P, Mailhot T, Riley D, et al. The RUSH exam: rapid ultrasound in shock in the evaluation of the critically lll. *Emerg Med Clin North Am*. 2010;28(1):29-56, vii.
20. Whitson MR, Mayo PH. Ultrasonography in the emergency department. *Crit Care*. 2016;20(1):227.
21. Lichtenstein D, Goldstein I, Mourgeon E, et al. Comparative diagnostic performances of auscultation, chest radiography, and lung ultrasonography in acute respiratory distress syndrome. *Anesthesiology*. 2004;100(1):9-15.
22. Lane AB, Petteys S, Ginn M, et al. Clinical importance of echogenic swirling pleural effusions. *J Ultrasound Med*. 2016;35(4):843-847.
23. Ngaage DL, Cowen ME. Right ventricular needle embolus in an injecting drug user: the need for early removal. *Emerg Med J*. 2001;18(6):500-501.
24. Peterson TC, Pearson C, Zekaj M, et al. Septic arthritis in intravenous drug abusers: a historical comparison of habits and pathogens. *J Emerg Med*. 2014;47(6):723-728.
25. Costantino TG, Roemer B, Leber EH. Septic arthritis and bursitis: emergency ultrasound can facilitate diagnosis. *J Emerg Med*. 2007;32(3):295-297.
26. Schluger NW, El-Bassel N, Hermosilla S, et al. Tuberculosis, drug use and HIV infection in Central Asia: an urgent need for attention. *Drug Alcohol Depend*. 2013;132 (Suppl 1):S32-S36.
27. Bouscaillou J, Evanno J, Proute M, et al. Prevalence and risk factors associated with HIV and tuberculosis in people who use drugs in Abidjan, Ivory Coast. *Int J Drug Policy*. 2016;30:116-123.
28. Murphy SL, Xu J, Kochanek KD, et al. Deaths: final data for 2015. *Natl Vital Stat Rep*. 2017;66(6):1-75.
29. Kendall CE, Boucher LM, Mark AE, et al. A cohort study examining emergency department visits and hospital admissions among people who use drugs in Ottawa, Canada. *Harm Reduct J*. 2017;14(1):16.
30. Broz D, Wejnert C, Pham HT, et al. HIV infection and risk, prevention, and testing behaviors among injecting drug users – National HIV Behavioral Surveillance System, 20 U.S. cities, 2009. *MMWR Surveill Summ*. 2014;63(6):1-51.
31. Moschella PC, Hart KW, Ruffner AH, et al. Prevalence of undiagnosed acute and chronic HIV in a lower-prevalence urban emergency department. *Am J Public Health*. 2014;104(9):1695-1699.
32. Patel EU, Laeyendecker O, Hsieh YH, et al. Parallel declines in HIV and hepatitis C virus prevalence, but not in herpes simplex virus type 2 infection: a 10-year, serial cross-sectional study in an inner-city emergency department. *J Clin Virol*. 2016;80:93-97.
33. White DA, Anderson ES, Pfeil SK, et al. Results of a rapid hepatitis C virus screening and diagnostic testing program in an Urban Emergency Department. *Ann Emerg Med*. 2016;67(1):119-128.
34. Anderson ES, Pfeil SK, Deering LJ, et al. High-impact hepatitis C virus testing for injection drug users in an urban ED. *Am J Emerg Med*. 2016;34(6):1108-1111.
35. Lyons MS, Kunnathur VA, Rouster SD, et al. Prevalence of diagnosed and undiagnosed hepatitis C in a Midwestern Urban Emergency Department. *Clin Infect Dis*. 2016;62(9):1066-1071.
36. Kievlan DR, Gukasyan M, Gesch J, et al. Clinical profile of injection drug users presenting to the ED. *Am J Emerg Med*. 2015;33(5):674-676.
37. Palepu A, Tyndall MW, Leon H, et al. Hospital utilization and costs in a cohort of injection drug users. *CMAJ*. 2001;165(4):415-420.
38. Cresti A, Chiavarelli M, Scalese M, et al. Epidemiological and mortality trends in infective endocarditis, a 17-year population-based prospective study. *Cardiovasc Diagn Ther*. 2017;7(1):27-35.
39. Kaye KS, Patel DA, Stephens JM, et al. Rising United States hospital admissions for acute bacterial skin and skin structure infections: recent trends and economic impact. *PLoS One*. 2015;10(11):e0143276.
40. McDermott KW, Elixhauser A, Sun R. Trends in Hospital Inpatient Stays in the United States, 2005–2014. HCUP Statistical Brief #225. 2017; https://www.hcup-us.ahrq.gov/reports/statbriefs/sb225-Inpatient-US-Stays-Trends.pdf. Accessed April 8, 2019.
41. Singh JA, Yu S. The burden of septic arthritis on the U.S. inpatient care: a national study. *PLoS One*. 2017;12(8):e0182577.

AUTHOR BIOGRAPHY

David C. Pigott, MD, is a Professor of Emergency Medicine and Co-Director of the Emergency Ultrasound program at the University of Alabama at Birmingham.

How to cite this article: DeMasi SC, Goyack LE, Shufflebarger EF, et al. Clinical ultrasonography in patients who inject drugs (the CUPID protocol): an illustrated case series. *JACEP Open*. 2020;1:244–251. https://doi.org/10.1002/emp2.12028