



Review

Point-of care ultrasound for the diagnosis and management of infections in immunocompromised patients and HIV/AIDS



Ecografía a pie de cama en el diagnóstico y manejo de las infecciones en pacientes inmunodeprimidos y VIH/sida

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ABSTRACT

Point-of-care ultrasound (POCUS) has become an essential tool in the diagnosis and management of infections in immunocompromised patients, including those with HIV. Despite the existence of several ultrasound protocols, an infection-specific protocol has not yet been developed. In immunocompromised patients, POCUS allows early identification of infectious processes. Ultrasound findings may not differ from those of the general population, but their interpretation does. They are more prone to infection by unusual microorganisms, involvement of unusual territories and formation of abscesses or masses of infectious origin. It is particularly useful for identifying signs of infection, such as consolidations and effusions. In immunocompromised patients, its usefulness varies according to the level of immunosuppression, being especially valuable in the identification of opportunistic infections. Including HIV, transplanted, hematological or autoimmune diseases patients, it facilitates a rapid and accurate assessment, guiding diagnostic and therapeutic procedures.

RESUMEN

La ecografía a pie de cama (*point-of-care ultrasound* [POCUS]) se ha convertido en una herramienta esencial en el diagnóstico y tratamiento de las infecciones en los pacientes inmunodeprimidos, incluidos aquellos con VIH. Pese a la existencia de múltiples protocolos ecográficos, aún no se ha desarrollado uno específico en enfermedades infecciosas. En los pacientes inmunodeprimidos el POCUS permite la identificación temprana de complicaciones infecciosas. Pese a que los hallazgos ecográficos pueden resultar similares, su utilidad e interpretación pueden diferir de las del paciente inmunocompetente. Se trata de pacientes con una mayor propensión a padecer infecciones por microorganismos poco frecuentes, afección de territorios inusuales y propensos a la formación de abscesos o masas de origen infeccioso. POCUS es especialmente útil para identificar signos de infección, como consolidaciones y derrames. En pacientes inmunodeprimidos, su utilidad varía según el nivel de inmunosupresión, siendo especialmente valioso en la identificación de infecciones oportunistas. En pacientes VIH, trasplantados, hematológicos o con enfermedades autoinmunes, facilita una evaluación rápida y precisa, orientando procedimientos diagnósticos y terapéuticos.

Introduction

The use of point-of-care ultrasound (POCUS) in the field of infectious diseases (ID) has been progressively implemented to become a very useful tool in both diagnosis and clinical decision making. It is a simple, safe and non-invasive technique that can be used by non-

radiologists with special interest in the field of infections in HIV-infected or immunocompromised patients.¹

Several ultrasound protocols have been developed in recent years; however, no specific or targeted ultrasound protocol has yet been designed for infectious diseases. Infections in immunocompromised or chronically HIV-infected patients remain a diagnostic and therapeutic challenge.² The origin of sepsis, bacteraemia, the focus of the infection and/or the extent of the infection will sometimes require expensive imaging methods that are difficult to acquire. This will be particularly

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important in healthcare environments with fewer material, economic or personal resources. The speed of diagnosis of multi-organ ultrasound “at the bedside”, always complementary to clinical assessment, will determine the prognosis of many patients, without forgetting the importance of its use not only for the visualization of the potential infectious focus but also to assist in the performance of echo-guided procedures.³

Although POCUS is extremely useful for evaluating signs of possible infection (consolidations, effusions, collections) complementing the classic clinical assessment, like other imaging tests, it cannot identify the aetiological agent with certainty, so it must always be integrated with knowledge of the probable diagnoses based on the type and degree of immunosuppression, as well as microbiological tests.⁴ Furthermore, in some cases its sensitivity may be limited compared to more advanced imaging techniques such as high-resolution tomography or magnetic resonance imaging, especially in small or deep lesions. Further studies on the diagnostic accuracy of POCUS specifically targeted at transplant patients are needed.⁵

Considerations for POCUS in immunocompromised patients

The immunocompromised patient encompasses a wide variety of diseases which presents a quantitative or qualitative alteration of the immune response, predisposing the patient to opportunistic infections, severe or recurrent infections, and certain types of neoplasms. This immunosuppression can be primary (congenital) or secondary (acquired), with the latter being much more common in clinical practice and with sometimes overlapping POCUS findings. However, we believe it is worth highlighting the particularity of several common cases of immunosuppression, such as HIV patients, transplant recipients, patients with haematological malignancies or with autoimmune, rheumatic or inflammatory diseases (Table 1).

Although the literature specific to infectious diseases in this particular setting is sparse, POCUS has a significant potential role that goes beyond a first approach to syndromic diagnosis, and extends to guiding procedures such as thoracentesis, pericardiocentesis and abscess drainage.¹ In terms of opportunistic infections, POCUS has the advantage of allowing a multi-organ assessment to be carried out at the same time, identifying other data that may lead to a greater suspicion of disseminated infection.

Sepsis and shock

As infections in immunocompromised patients are one of the most common scenarios, the most serious complication that must be identified as soon as possible is septic shock.

In immunosuppressed patients undergoing chemotherapy or biological therapies, fever may be the only sign of infection, being associated with high mortality. By contrast, more than one third of infections can occur without fever, especially in fungal infections, while up to one in five times fever will have a non-infectious cause in transplant patients.⁶

In a context where speed of diagnosis is essential, POCUS allows a faster diagnostic approach in a few minutes, compared to other imaging techniques.⁷ In these patients, in the absence of clear guiding symptoms, the ultrasound examination needs to be comprehensive and involve several systems. Several studies have shown the usefulness of multi-organ ultrasonography.⁸ The scanned areas should include pulmonary, cardiac and abdominal. Although there is no specific protocol, the ACES (abdominal and cardiac evaluation with sonography in shock) and RUSH (rapid ultrasound in shock) protocols are the most frequently used. Their usefulness is based on the identification of the type of shock, usually distributive in a patient with sepsis and fever, in the finding of the infectious focus (pulmonary consolidation, liver abscess, etc.), also allowing interventions such as drainage of the infectious focus, obtaining a sample or catheterisation and monitoring of the septic patient through haemodynamic parameters.¹

The RUSH protocol for evaluating sepsis requires careful consideration. Firstly, recognition of the type of shock is based on three key elements. These are the pump, the tank and the pipes, meaning the potential causes of hypotension within the heart, vascular volume and the vessels are examined. This evaluation requires images of the heart, the inferior vena cava (IVC), abdominal Morinson's, the aorta and the lungs.⁹ Secondly, sepsis is a dynamic process. Initially, there is a hypovolaemic phase characterised by pulmonary A-lines, a hyperdynamic heart and a depleted IVC. This is followed by, the more frequent, distributive phase characterised by diffuse B-lines, due to acute respiratory distress syndrome (ARDS), a hyperdynamic heart and an increased IVC diameter. Finally, there can be a cardiogenic phase characterised by B-lines predominant in the lung bases or pleural effusion, a hypodynamic heart with diastolic dysfunction or a reduced left ventricle ejection fraction, an increased IVC diameter and abdominal free fluid.¹⁰

POCUS also provides dynamic measures to guide fluid resuscitation during sepsis, such as evaluating cardiac output through EPSS (E-point septal separation), FS (fractional shortening) or LVOT VTI (left ventricular velocity–time integral), assessing fluid responsiveness through LVOT VTI, filling pressures, right ventricular preload (inferior vena cava and internal jugular vein assessment), left ventricular preload (extravascular lung water – pathological B-lines) and visceral congestion VExUS (venous excess ultrasound).¹¹

HIV/AIDS patients

The usefulness of ultrasound in the management of infectious pathology in HIV patients will depend on the degree of cellular immunosuppression (i.e. total CD4 lymphocytes). Non-immunosuppressed HIV patients (CD4 > 500 cells/mm³) will generally have infections similar to those in the immunocompetent population. However, when CD4 cells are below 250 cells/mm³, there are several opportunistic infections (OLs) associated with HIV in which POCUS will be of special interest both in the diagnostic evaluation and in the identification of complications associated with AIDS or its treatment. There are many microorganisms responsible for HIV-associated OLs (such as *Pneumocystis jirovecii*, *Cryptococcus*, *Toxoplasmosis*, *Aspergillus* or *Nocardia*) and one in every three patients HIV will be affected by OLs. After oro-pharyngeal candidiasis and cutaneous affections, pneumonia is the most prevalent infection, with *Pneumocystis* and *Mycobacterium tuberculosis* being the most noteworthy pathogens.¹² Also, in the context of immunosuppression, are responsible for the development of hepatosplenomegaly, generalised or localised lymphadenopathy, intra-abdominal, cutaneous or subcutaneous masses. The presence or absence of these findings will be fundamental in the differential diagnosis of an immunocompromised HIV patient with suspected infectious pathology. The identification of these findings will be possible through the application of POCUS at the bedside as it will be able to guide the diagnosis, confirm the clinical suspicion and guide us to obtain microbiological and histopathological samples in many cases, in a direct, inexpensive and fast way.¹³

Transplant patients

Infections represent a major cause of morbidity and mortality in the solid organ transplant (SOT) patient. A rapid and accurate assessment is therefore necessary to initiate timely treatment. However, diagnosis is a diagnostic challenge where the clinical presentation may be less florid and laboratory data less accurate.

When interpreting the usual POCUS findings in the differential diagnosis, some aspects specific to the transplant recipient must be considered. The time of onset of the most common infections depends on the post-transplantation risk factors: in general, in the first month post-transplant, nosocomial and post-surgical infections or donor-transmitted infections predominate; later and up to the sixth or twelfth month post-transplant, opportunistic infections (such as cytomegalovirus infection,

Table 1

Summary of the utility of point-of-care ultrasound (POCUS) in immunocompromised patients by disease.

Immunocompromised host	POCUS
HIV	<ul style="list-style-type: none"> - Identification of opportunistic infections such as pneumonia by <i>Pneumocystis jirovecii</i> and tuberculosis. - Evaluation of lymphadenopathies to differentiate between infectious, inflammatory, or neoplastic processes.
Transplant	<ul style="list-style-type: none"> - Detection of hepatosplenomegaly, intra-abdominal masses, cutaneous or subcutaneous masses. - Detection of nosocomial, opportunistic, and community infections based on post-transplant time. - Identification of post-transplant abdominal complications such as abscesses, hematomas, and lymphoceles.
Hematologic malignancy	<ul style="list-style-type: none"> - Detection of infectious endocarditis, allowing identification of valvular vegetations in patients with bacteraemia or candidemia. - Evaluation of hepatomegaly, splenomegaly, free fluid, abscesses, and collections. - Anticipation of pulmonary complications in patients undergoing hematopoietic cell transplantation through serial ultrasound.
Autoimmune, rheumatic or inflammatory diseases	<ul style="list-style-type: none"> - Identification of joint effusions and guidance for arthrocentesis. - Evaluation of pulmonary infections, endocarditis, abscesses, and fluid collections. - Detection of lymphadenopathies that may be manifestations of systemic infections or infectious complications in patients undergoing biological treatments.

P. jirovecii, *Aspergillus* or *Nocardia*) arise due to the increased state of immunosuppression, and whose incidence is minimized with the administration of prophylactic treatment; and beyond 6–12 months, community infections and other viral infections such as late-onset cytomegalovirus (CMV) disease, BK polyomavirus infection, papillomavirus or Epstein-Barr virus, the latter associated with post-transplant lymphoproliferative disorders (PTLD), are on the rise.⁶ *M. tuberculosis* infection is 30–100 times more frequent in this population than in the general population, usually during the first-year post-transplantation. Although pulmonary infection is the most common form of presentation, extrapulmonary and disseminated forms may also occur.¹⁴ The respiratory system is the most common site of infection in heart and lung transplant recipients, and the second most common site of infection in liver transplant recipients. Similarly, solid organ transplant recipients may develop multiple post-transplant abdominal complications. They may develop surgical site infections and superinfections of common post-surgical collections such as haematomas, lymphoceles or urinomas. Patients with thrombosis, graft dysfunction or failure, among others, or those requiring re-interventions or re-transplantation are at even higher risk.¹⁵ In addition to the most common pathology, opportunistic infections should be taken into account.¹⁴

Haematological malignancies

Infections are a major cause of mortality in hematology patients, especially those having undergone allogenic hematopoietic stem cell transplantation. Like HIV/AIDS patients the degree of immunosuppression is determinant. Neutropenia predisposes severe bacterial and fungal infections, and an impaired T-cell function increases the risk of fungal and viral infections. Infections in hematologic patients are very common and the mortality in neutropenic fever patients is around 20% in patients with lung infiltrates, 35% in severe sepsis, and 50% in patients with septic shock.¹⁶

When performing POCUS, in search of an infectious focus, pulmonary infections are one of the most common. Secondly complications associated with central venous catheters, both local, cellulitis and bacteraemia, which many of these patients have. Endocarditis, although rare, has a particular impact on these patients.^{17,18}

Autoimmune, rheumatic or inflammatory diseases

In patients with autoimmune, rheumatic or inflammatory diseases, the disease itself and the use of therapies such as chronic treatment with corticosteroids (≥ 20 mg/day of prednisone or equivalent for more than 2–4 weeks) or immunosuppressants (biologicals, antimetabolites, calcineurin inhibitors, etc.) favor the appearance of infectious complications.

Once again, pneumonia, particularly bacterial pneumonia, will be the most common infection, followed by urinary tract infections and skin and soft tissue infections. More profound immunosuppression can lead to infections caused by filamentous fungi and *P. jirovecii*. The risk of these infections is increased in the first few months of treatment.^{19,20}

POCUS has particular interest in patients with pathologies such as rheumatoid arthritis, where chronic inflammation can mask signs of acute infection and it allows us to identify joint effusions and guide arthrocentesis.²¹ Allows detection of lymphadenopathies, which may be the manifestation of systemic infections or local complications in patients undergoing biologic therapies.^{22,23}

POCUS in immunocompromised patients

Given their immunosuppressed state, several specific circumstances have to be considered in relation to the ultrasound findings of the scanned regions (Table 2).

Nervous system

Immunosuppressed patients have a higher prevalence of infections of the central nervous system (CNS) and by pathogens that would not normally cause them. The role of POCUS in CNS infections is well established in the paediatric population, where the anterior fontanel provides an adequate ultrasound window until its closure at 19 months, allowing the diagnosis of meningitis, ventriculitis, hydrocephalus, abscesses, empyema and abscesses.²⁴

In the adult population its use is more limited, although we can highlight several initiatives such as Neuro-POCUS, which advocate its implementation in the neurological critical patient. Depending on the clinical situation, it includes a series of ultrasound findings related to the underlying pathology.²⁵

At the infectious level, in cases of meningitis or encephalitis, local increases in blood flow velocity, increased pulsatility and resistance indices in the intracranial arteries are to be expected. It is also useful in the diagnosis and monitoring of intracranial hypertension by ultrasound measurement of the optic nerve sheath, such as intracranial abscesses or cryptococcal meningitis. Values above 6 mm may suggest intracranial hypertension, although the correlation between intracranial hypertension and opening pressure is variable (Fig. 1).²⁶

Cryptococcus can cause serious infections in the immunocompromised patient, particularly central nervous system involvement in HIV patients. Management of these patients requires monitoring of intracranial pressure by lumbar puncture to maintain the opening pressure < 20 cm H₂O. Measurement of the optic nerve sheath may be useful in monitoring intracranial pressure, as well as in locating the optimal puncture site.

Table 2

Summary of the utility of point-of-care ultrasound (POCUS) in immunocompromised patients by systems.

System	POCUS
Nervous system	Evaluation of intracranial pressure and puncture place.
Respiratory system	Identification of pneumonias, pleural effusions, viral, fungal lung infections, pulmonary embolism and tuberculosis.
Cardiovascular	Detection of endocarditis, valvular vegetations, pericardial effusions and cardiac masses.
Abdominal	Diagnosis of intra-abdominal infections, hepatic and renal abscesses, and detection of ascites.
Rheumatological	Identification of joint effusions, infectious arthritis, and lymphadenopathies.
Lymphatic	Evaluation of lymphadenopathies to differentiate between infectious, inflammatory, or neoplastic processes.
Skin and soft tissues	Diagnosis of cellulitis, abscesses, and necrotizing fasciitis.



Fig. 1. Point of care optic nerve sheath ultrasound (ONSUS) is a bedside practice that can be used to evaluate for increased intracranial pressure. Eyeball. Lens is observed firstly followed by the vitreous humour, then the retina and the optic nerve (yellow) together with its sheath at the deepest level. The transverse thickness of the optic nerve (line) is measured at 3 mm from the blind spot (arrow).

Furthermore, it is employed in the identification of the area for lumbar puncture and it also allows us to detect local complications, such as ventricular shunt valve infections (Fig. 2).²⁷

Cardiovascular

The detection of infective endocarditis by POCUS has shown good sensitivity, allowing the identification of valvular vegetations in patients with bacteraemia or candidaemia, infections of relevance in haematological patients.²⁸

Echocardiography of the immunocompromised patient does not differ significantly from that of the immunocompetent. However, it is of particular relevance since these patients are particularly predisposed to bacteraemia and candidaemia, and therefore, in an infectious context, one should look particularly closely for data suggesting endocarditis such as vegetations, valvular insufficiency, cardiac structural abnormalities, but also hepatomegaly, splenomegaly and septic emboli at the hepatic, splenic and renal level.²⁸

It is also possible to detect pericardial masses or effusions, which in this context may be particularly related to infections with tuberculous and non-tuberculous mycobacteria, *P. jirovecii*, Kaposi's sarcoma and lymphomas.²⁹

Lungs

Ultrasound may be valuable in the evaluation of pulmonary infections in the immunocompromised patient, although the literature is still scarce in this clinical setting.³⁰ It can detect and characterize focal B-lines, subpleural, pulmonary and other peripheral areas with "hepatization" of the lung parenchyma, where lung ultrasound has a higher sensitivity for the diagnosis of pneumonia than conventional chest

radiography.³¹ POCUS typically shows bilateral multifocal B-lines whose number correlates with severity and may result in a "white lung" appearance.¹ A clear example of this has been its use in the evaluation of patients with COVID-19.³²

POCUS is a test with a very high sensitivity and specificity in the detection of pleural effusion, being also more sensitive than conventional chest radiography. Ultrasound allows the type of effusion to be checked and guides the thoracentesis procedure, increasing its safety and allowing the analysis of pleural fluid and the microbiological identification of less common pathogens (Fig. 3).³³

Lung ultrasound may show patterns such as bilateral B-lines accompanied by subpleural hypercoherent granularity in case of miliary tuberculosis.^{33,34} The presence of B lines and infiltrates should not only raise suspicion of bacterial infection but also of fungal and mycobacterial infections, especially in the case of large consolidations or masses, which should increase the suspicion of fungal, bacterial or PTLD (post-transplant lymphoproliferative disorder). Other non-infectious processes such as organized pneumonia, drug toxicity or acute rejection in lung transplantation should be included in the differential diagnosis.³⁴

P. jirovecii can cause lung infection and respiratory failure and it is a common pathogen in HIV, haematological or autoimmune immunocompromised patients. The application of pulmonary POCUS can warn us of its presence. Regarding other opportunistic infections in immunosuppressed patients, different ultrasound findings have also been described in POCUS of *P. jirovecii* pneumonia.³⁵ The presence of B-lines, subpleural consolidations and cystic changes are suggestive of *P. jirovecii*, the latter finding with lower sensitivity but higher specificity, while parenchymal consolidations and pleural effusion should suggest other pathologies (Fig. 1 Supplementary materials).³⁶ Ultrasonographic descriptions of other fungal lung infections in immunosuppressed patients are still very scarce. The radiological presentation may differ depending on the type

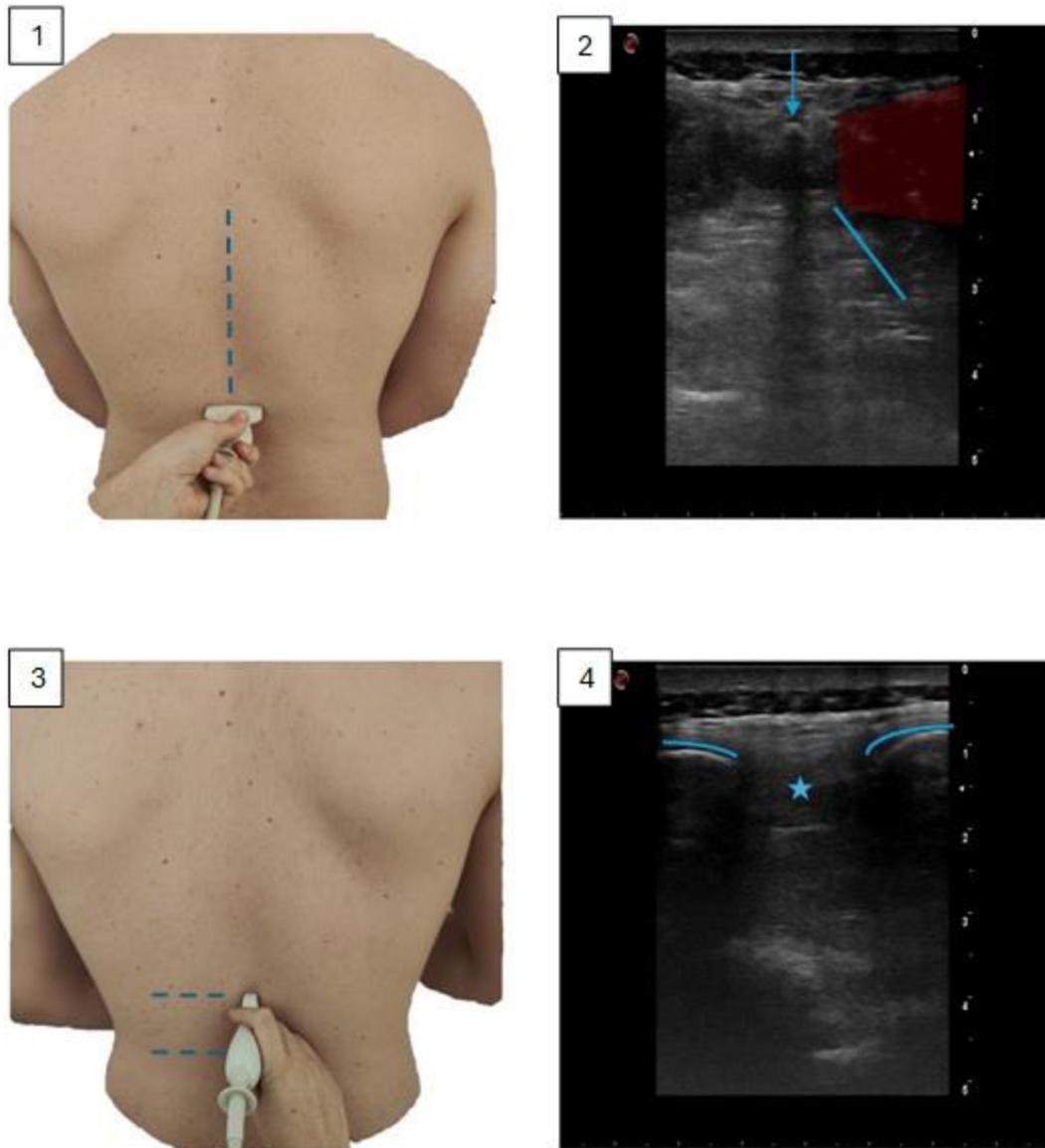


Fig. 2. POCUS guided lumbar puncture. 1: Midline (line). 2: Spinous process (arrow). Paraspinal muscle (red shadow). Lamina and transverse process (line). 3: Marked spinous processes (lines). Intervertebral space between them. 4: Spinous processes (line). Intervertebral space between them (asterisk).

and degree of immunosuppression. Ultrasound findings include both hypodense nodules with a hyperechogenic ring and hypoechoic nodules with a hyperechogenic ring, as well as heterogeneous subpleural consolidations, sometimes with pleural effusion. Mycetoma may be detected as a central hyperechoic roundish area with air extension to the peripheral anechoic rim.^{30,34,37}

Tuberculosis (TB) remains a highly prevalent infection in HIV-infected and immunocompromised populations. Ultrasound is a very useful tool for the diagnosis and management of the different forms of pulmonary and extrapulmonary TB. An ultrasound protocol called FASH (focused assessment with sonography for HIV-associated TB) has been developed for the ultrasound assessment of TB changes in areas of high TB endemicity and HIV co-infection, with the aim of being used by physicians without extensive experience with the ultrasound technique. This protocol describes how the evaluation should be performed, helps to identify which findings are normal or pathological, and attempts to approximate an initial interpretation in order to be able to make diagnostic and therapeutic decisions. This protocol seeks to detect intrathoracic or intra-abdominal effusions or serositis (pleural effusion, pericardial effusion and ascites), presence or absence of

lymphadenopathy, as well as solid organ abscesses, mainly in the liver and spleen (Table 3).³⁸

For those patients with hematological malignancies, the use of serial POCUS, using LUS (lung ultrasound) protocol every two or three days, can help to anticipate complications in patients undergoing haematopoietic cell transplantation (HCT). Multiple B lines (scores > 3) are associated with infectious pulmonary complications and graft-versus-host disease. It is a technique with a higher sensitivity and specificity than conventional radiography and lower than computed tomography (CT), with the advantage of being able to be performed serially, without mobilizing or delaying the patient and without subjecting the patient to radiation.³⁹

Abdomen

In intra-abdominal infection, POCUS can be equally valuable in the immunosuppressed patient. In addition to being a useful tool in the diagnosis of more common intra-abdominal infections as extensively documented in the immunocompetent population (such as appendicitis, diverticulitis, colitis, cholecystitis or urinary tract infections), POCUS

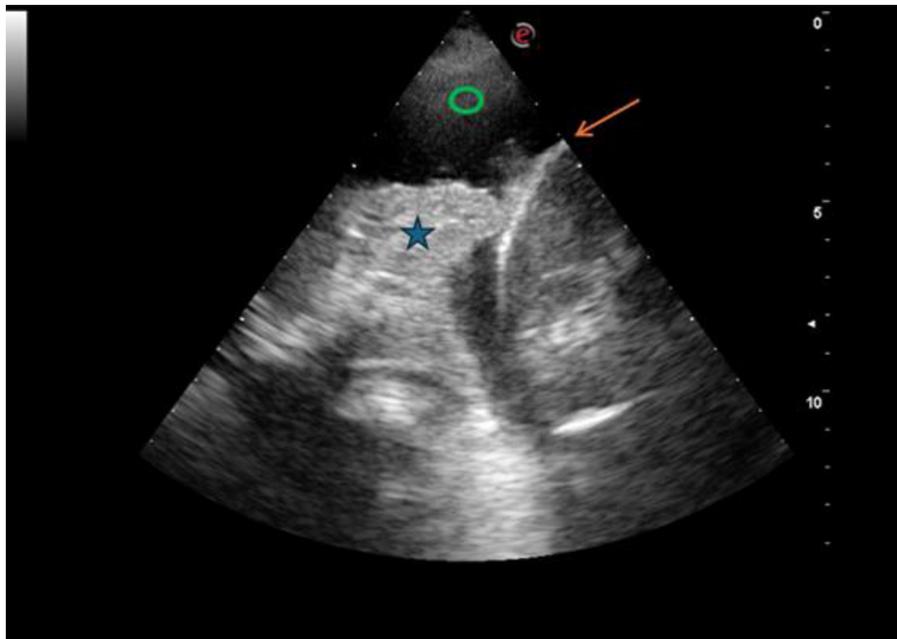


Fig. 3. Pleural effusion and pulmonary hepatisation. On the left, a hepatized lung (asterisk) can be seen, separated from the diaphragm (arrow) on the right by a hypoechoic pleural effusion (circle).

Table 3

Clinical question addresses by FASH.

FASH-basic	Clinical questions	FASH-plus	Clinical questions
Presence of pericardial effusion	Pericardial TB	Presence of periportal/para-aortic lymph nodes	Abdominal TB
Presence of pleural effusion	Pleural TB	Presence of focal liver lesion	Liver abscess TB
Presence of ascites	Abdominal TB	Presence of focal splenic lesions	Disseminated TB

Adapted from Heller et al.³⁸

FASH: focused assessment with sonography for HIV-associated TB; TB: tuberculosis.

can also be a useful tool in the diagnosis of intra-abdominal infections^{1,40} can detect early liver, renal or perirenal abscesses, and can detect, for example, other post-transplant complications that can lead to a differential diagnosis with infectious processes.⁴¹ This is especially relevant in abdominal transplants such as liver or reno-pancreatic transplantation, where post-surgical or graft-related abscesses may occur. Ultrasound can also guide the drainage of these abscesses.¹

POCUS is very useful in the detection of free fluid. The presence of ascites, visible ultrasonographically with high sensitivity, may be a sign of intra-abdominal infection or a manifestation of diseases such as peritoneal tuberculosis.⁴² Ultrasound can guide diagnostic paracentesis. It can also assess at the same time other findings suggestive of extrapulmonary tuberculosis, which have proven very useful in immunosuppressed patients with HIV infection.⁴³ Thus, the FASH approach can be very useful in high TB prevalence settings: the presence of adenopathy, pericardial effusion, pleural effusion and ascites are common manifestations of extrapulmonary TB.⁴⁴ In cases of abdominal TB, peripancreatic and mesenteric lymphadenopathies are frequently observed, while iliac and lumbar regions are less commonly affected. Characteristically, lymphadenopathies may show sonographic data of necrosis and posterior enhancement or hyperechogenicity due to calcifications.⁴⁵ POCUS can also monitor treatment response.⁴⁶

Assessment of the liver and spleen can also be useful, not only to confirm possible megalithia, but also to detect lesions indicative of less common entities in non-immunocompromised patients. Thus, the presence of multiple small hypoechoic splenic lesions of between 0.5 and 1 cm compatible with microabscesses may point to tuberculosis (or to

a lesser extent to other non-tuberculous mycobacterial infections or, in patients from endemic areas, to endemic mycoses or melioidosis).³⁸

In the renal transplant patient, POCUS can be useful in the detection of abscesses, pyelonephritis, or pyonephrosis and can assess both the renal graft and the native kidney. It can also find abscesses in other organs such as the prostate, or detect obstructive uropathy, lithiasis, lymphoceles, haematomas or abscesses, the latter with a thick wall and being able to visualise internal echoes and septa (Fig. 2 Supplementary materials). POCUS can also guide the puncture of the collection under study.⁴¹

Lymphadenopathies

Lymph nodes can appear in numerous areas, although it is those located in the head and neck, axillae and inguinal region that are of particular interest in the ultrasound examination. Lymph node diseases, in general, are characterized ultrasonographically by an increase in size and a decrease in echogenicity.⁴⁷

Firstly, it is important to recognize the morphology of a normal lymph node. They usually have an echogenic hilum with vascular flow, and an oval morphology, with a length-to-width ratio greater than two. Reactive lymph nodes are a very frequent ultrasound finding in this population. The morphology is typically oval with smooth borders. They become somewhat more hypoechoic, although morphologically they maintain their homogeneity with the presence of a “band” which is usually the hilum with small vascularization and fat (Fig. 3 Supplementary materials).

Sometimes there are non-specific inflammatory infections (non-specific acute adenitis) whose ultrasound morphology is very similar to that of reactive adenitis, maintaining differentiation with respect to the surrounding tissues, although sometimes the hilum is not preserved. When the inflammation becomes chronic, the size of the lymph node usually decreases considerably, turning into hypoechoic, oval images with well-defined borders.

The association of suppurative adenitis is very frequent in immunosuppressed patients. The lymph node is enlarged, with fluid content inside (cystic or hypo/anechoic appearance) and usually with adjacent inflammatory signs (poorly demarcated margins), and colour Doppler shows increased peripheral vascularisation.

The presence of lymphadenopathy in HIV patients is generally due to activation of the immune system and lymphocyte proliferation at the lymph node level. There are many causes of lymphadenopathy and sometimes they may overlap. Opportunistic infections, inflammatory processes and neoplasms are the main etiologies that can be observed at any time during HIV infection, regardless of its stage. POCUS is a non-invasive and radiation-free technique that is very useful in discriminating the nature of lymphadenopathy. In a first step, it is important to differentiate whether it is an infectious, inflammatory or neoplastic process. A combined nomogram using ultrasound parameters including age, number of affected lymphatic regions and vascularization or intranodal Doppler patterns has been proposed in order to improve the diagnostic accuracy of ultrasound lymph node diagnosis in an objective manner.⁴⁸ Their study showed that older age, having color Doppler grade 2–3 (according to Adler's criteria) and having only one lymph node region affected were independent risk factors for the malignancy criterion.⁴⁹

Lymphadenopathies affected by granulomatous infections, mainly tuberculosis, have a variable morphology and appearance, but can be confused with other lymphadenopathies such as metastases. They manifest themselves with a significant increase in size, cortical deformation, poorly demarcated contours and what is most striking is the area of necrosis within them. In chronic stages, calcium may be deposited in the lymph nodes. Therefore, although the ultrasound appearance of lymphadenitis due to tuberculosis can be very variable and non-specific, ultrasound will not only allow direct observation of the lesion, but will also help to obtain tissue or a sample inside the lesion for subsequent analysis and interpretation (Fig. 4 Supplementary materials).⁵⁰

One of the main challenges is to differentiate between benign and malignant lymphadenopathy. Although ultrasonographic differentiation will generally be very difficult (given the wide heterogeneity of causes and clinical pictures), the ultrasonographic shape of the lymphadenopathy may be useful in a first approximation: in general, ovoid morphology is usually associated with benign processes while spherical morphology is associated with malignancy. Loss of definition of the hilum may also be suspicious for malignancy, as well as the presence of ill-defined borders.

It should be borne in mind that in the immunocompromised patient, lymphadenopathies in the pathological range and masses may be more frequently due to infectious diseases than in the general population.

Skin and soft-tissue

Patients with impaired immunity are at an increased risk of skin and soft tissue infections caused by unusual microorganisms, such as fungi and mycobacteria.⁵¹

Synovitis, bursitis, or arthritis are common signs. POCUS can help identify them, as well as obtain material to rule out or confirm suspected septic arthritis (Fig. 5 Supplementary materials).

Cellulitis is one of the main pathologies whose ultrasound diagnosis will vary from diffuse oedema of the skin or subcutaneous cellular tissue to the presence of perifascial fluid (a finding known as “cobblestone imaging”). Ultrasound will monitor the evolution of the infection and rule out the presence of other complications such as

necrotising fasciitis, pyomyositis and abscess formation. A high-frequency linear probe is used for exploration by means of a longitudinal and a transverse plane (Fig. 6 Supplementary materials).⁵²

The ultrasound finding of the abscess is characterised by a localised collection, generally hypoechoic and well-defined, although on occasions its echogenicity may be altered by the presence of *debris* or septa, which is suggestive of chronicity. The presence of posterior acoustic reinforcement is an important diagnostic feature. The presence of fluid accumulation along the fascia may be suggestive of necrotizing fasciitis (Table 1 Supplementary materials).⁵³

Catheter-related Infection

Immunocompromised patients frequently undergo the implantation of invasive devices such as catheters, dialysis catheter, central venous catheters, implantable ports, or other chronic devices. Their immunosuppressed state, combined with the breakage of natural protective barriers, leads to an increased risk of infection.⁵⁴ Catheter-related infections (CRI) and central line-associated bloodstream infection (CLABSI) are frequent complications of immunocompromised patients associated with high morbidity and mortality.⁵⁵

Prior to the development of sepsis and shock, POCUS can provide us with findings that alert of the presence of infectious complications. Depending on the type of catheter, the infection can be in either the exiting site, the tunnel or vessel and the intracavitary or intravascular space. The catheter should be traced along its subcutaneous path from one end to the other. This initial approach involves evaluating the subcutaneous course. Ultrasound findings that suggest infection include the presence of a thrombus, wall thickening, hyperechogenicity and fluid collection around the device.⁵⁶

The use of ultrasound to guide catheter implantation has been shown to reduce the incidence of both mechanical complications and infections.⁵⁷ Although the potential benefits of POCUS screening for signs of infection are promising, its effectiveness remains to be established.⁵⁸

Conclusion

In conclusion, the use of point-of-care ultrasound has established itself as a valuable tool in the management of infections in immunocompromised patients, including those with HIV/AIDS. Its ability to provide rapid and accessible diagnostic information is crucial in improving the clinical care of this vulnerable group. However, it is essential to remember that POCUS should be used as an adjunct to other diagnostic methods, as it cannot identify with certainty the etiological agent of infections.

In patients with HIV, the usefulness of POCUS varies according to the level of immunosuppression. Patients with CD4 counts above 500 cells/mm³ have infections similar to the general population, while those with CD4 counts below 250 cells/mm³ may develop opportunistic infections where ultrasound may be critical for diagnosis. For example, POCUS is especially useful in identifying infections such as *P. jirovecii* pneumonia and tuberculosis, the latter being a prevalent infection in HIV patients. In addition, ultrasound is a valuable tool for assessing lymphadenopathy in HIV patients, helping to differentiate between infectious, inflammatory and neoplastic processes.

In the transplant patient, POCUS facilitates rapid and accurate assessment, guiding diagnostic and therapeutic procedures. Identification of infections in these patients can be complicated by the atypical presentation of symptoms, and POCUS can be an essential tool to guide interventions such as thoracentesis, pericardiocentesis and abscess drainage. It is important to keep in mind that infections in transplant recipients may vary according to time post-transplantation and associated risk factors.

In patients with haematological malignancies, infections are a major cause of mortality. POCUS has proven to be effective in detecting

infective endocarditis, allowing the identification of valvular vegetations in patients with bacteraemia or candidaemia. In addition, serial ultrasound can help to anticipate pulmonary complications in patients undergoing haematopoietic cell transplantation.

In patients with autoimmune diseases, it allows early identification of complications, and at the joint level it allows visualisation of arthritis and guiding arthrocentesis to identify infectious arthritis.

Finally, it is crucial to maintain high standards of hygiene in the use of ultrasound equipment, especially in immunocompromised patients, to prevent the transmission of pathogens.

In conclusion, although POCUS offers significant advantages in the management of infections in immunocompromised patients, more research is needed to establish specific protocols and validate its efficacy in various infections.

Ethical considerations

The conduct of this review did not involve human participants.

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Conflict of interest

None declared.

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.1016/j.medcli.2025.107322>.

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