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Consensus Statement

^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT imaging for the evaluation of cardiovascular infection in the multimodality context

ASNC Imaging Indications (ASNC I^2) Series Expert Consensus Recommendations from ASNC, AATS, ACC, AHA, ASE, EANM, HRS, IDSA, SCCT, SNMMI, and STS

Jamieson M. Bourque,[1] Ulrika Birgersdotter-Green,[2] Paco E. Bravo,[3] Ricardo P.J. Budde,[4] Wengen Chen,[5] Vivian H. Chu,[6] Vasken Dilsizian,[5] Paola Anna Erba,[7] Cesia Gallegos Kattan,[8] Gilbert Habib,[9] Fabien Hyafil,[10] Yiu Ming Khor,[11] Jaimie Manlucu,[12] Pamela Kay Mason,[13] Edward J. Miller,[8] Marc R. Moon,[14] Matthew W. Parker,[15] Gosta Pettersson,[16] Robert D. Schaller,[17] Riemer H.J.A. Slart,[18] Jordan B. Strom,[19] Bruce L. Wilkoff,[20] Adam Williams,[22] Ann E. Woolley,[21] Brittany A. Zwischenberger,[22] Sharmila Dorbala[23]

From the [1]Cardiovascular Division and the Cardiovascular Imaging Center, Departments of Medicine and Radiology, University of Virginia Health System, Charlottesville, VA, USA, [2]Division of Cardiology, UC San Diego Health, San Diego, CA, USA, [3]Divisions of Nuclear Medicine, Cardiothoracic Imaging and Cardiovascular Medicine, Director, Nuclear Cardiology and Cardiovascular Molecular Imaging, Hospital of the University of Pennsylvania, Philadelphia, PA, USA, [4]Department of Radiology and Nuclear Medicine, Erasmus MC, University Medical Center, Rotterdam, the Netherlands, [5]University of Maryland School of Medicine, Department of Diagnostic Radiology and Nuclear Medicine, Baltimore, MD, USA, [6]Division of Infectious Diseases, Duke University School of Medicine, Durham, NC, USA, [7]Department of Medicine and Surgery University of Milano Bicocca and Nuclear Medicine, ASST Ospedale Papa Giovanni XXIII, Bergamo, Italy, [8]Nuclear Cardiology, Yale University School of Medicine, New Haven, CT, USA, [9]Cardiology Department, Hôpital La Timone, Marseille, France, [10]Nuclear Cardiology and Nuclear Medicine Department, DMU IMAGINA, Hôpital Européen Georges-Pompidou, University of Paris, Paris, France, [11]Department of Nuclear Medicine and Molecular Imaging, Singapore General Hospital, Singapore, [12]London Heart Rhythm Program, Western University, London Health Sciences Centre (University Hospital), London, Ontario, Canada, [13]Cardiovascular Medicine, University of Virginia Health System, Charlottesville, VA, USA, [14]Division of Cardiothoracic Surgery, Baylor College of Medicine, Houston, TX, USA, [15]Echocardiography Laboratory, Division of Cardiovascular Medicine, University of Massachusetts T.H. Chan School of Medicine, Worcester, MA, USA, [16]Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, Cleveland, OH, USA, [17]Department of Cardiac Electrophysiology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA, [18]Medical Imaging Centre, Department of Nucleare, Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, Groningen, the Netherlands, [19]Division of Cardiovascular Medicine, Beth Israel Deaconess Medical Center, Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology, Harvard Medical School, Boston, MA, USA, [20]Cardiac Pacing & Tachyarrhythmia Devices, Department of Cardiovascular Medicine, Professor of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, USA, [21]Division of Thoracic and Cardiovascular Surgery, Duke University Medical Center, Durham, NC, USA, [22]Brigham and Women's Hospital, Boston, MA, USA, and [23]Cardiovascular Imaging Program, Departments of Medicine and Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.

ABSTRACT

This document on cardiovascular infection, including infective endocarditis, is the first in the American Society of Nuclear Cardiology Imaging Indications (ASNC I^2) series to assess the role of radionuclide imaging in the multimodality context for the evaluation of complex systemic diseases with multi-societal involvement including pertinent disciplines. A rigorous modified Delphi approach was used to determine consensus clinical indications, diagnostic criteria, and an algorithmic approach to diagnosis of cardiovascular infection including infective endocarditis. Cardiovascular infection incidence is increasing and is associated with high morbidity and mortality. Current strategies based on clinical criteria and an initial echocardiographic imaging approach are effective but often insufficient in complicated cardiovascular infection. Radionuclide imaging with ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (CT) and single photon emission computed tomography/CT leukocyte scintigraphy can enhance the evaluation of suspected cardiovascular infection by increasing diagnostic accuracy, identifying extracardiac involvement, and assessing cardiac implanted device pockets, leads, and all portions of ventricular assist devices.

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This advanced imaging can aid in key medical and surgical considerations. Consensus diagnostic features include focal/multifocal or diffuse heterogenous intense ^{18}F-FDG uptake on valvular and prosthetic material, perivalvular areas, device pockets and leads, and ventricular assist device hardware persisting on non-attenuation corrected images. There are numerous clinical indications with a larger role in prosthetic valves, and cardiac devices particularly with possible infective endocarditis or in the setting of prior equivocal or non-diagnostic imaging. Illustrative cases incorporating these consensus recommendations provide additional clarification. Future research is necessary to refine application of these advanced imaging tools for surgical planning, to identify treatment response, and more.

KEYWORDS ^{18}F-fluorodeoxyglucose PET/CT; Appropriate use; Cardiovascular infection; SPECT/CT leukocyte scintigraphy; Infective endocarditis

(Heart Rhythm 2024;■:1–29)

ABBREVIATIONS ^{18}F-FDG = Fluorine-18 fluorodeoxyglucose; CIED = cardiovascular implantable electronic device; CTA = computed tomography angiography; ICD = implantable cardioverter defibrillator; IE = infective endocarditis; NVE = native valve endocarditis; PET = positron emission tomography; PVE = prosthetic valve endocarditis; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography; SPECT = single photon emission computed tomography; VAD = ventricular assist device (Heart Rhythm 2024;■:1–29)

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Background and aims

The incidence of cardiovascular infection in native and prosthetic valves, prosthetic material, and cardiovascular implantable electronic devices (CIEDs) is increasing. Valvular infective endocarditis (IE) is estimated to occur in 2-10 per 100,000 persons[1]; however, studies in the United States and elsewhere suggest the incidence is increasing due to expanding rates of implantation of cardiac and other vascular devices and the recent epidemic of injection drug use[2,3]. While native valve endocarditis (NVE) accounts for the majority (approximately 80%) of cases, prosthetic valves present unique considerations that affect diagnosis and management of infection, such as timing from implantation, type of prosthesis, endothelial injury during placement, and residual valvular regurgitation[4,5]. Valvular IE leads to significant morbidity[1] and is associated with an in-hospital mortality of approximately 20% and high costs[6–9].

CIEDs, ventricular assist devices (VADs), and other prosthetic materials are increasingly utilized in the contemporary treatment of cardiovascular diseases. Twelve-month incidence of CIED infection was 1.0-1.2% in two large contemporary randomized trial cohorts[4,10] but registries have found higher rates[5,11–14]. Confirmed diagnosis requires complete system extraction and prolonged antibiotic therapy with high mortality rates of more than 20% in patients with bacteremia or vegetations[13].

Cumulative vascular graft infection rates vary between 0.2 and 6.0% depending on the time period analyzed, and they are associated with high rates of mortality and reinfection[14]. Aggressive antibiotics are required and surgical revision is challenging. VADs have a high rate of infection (15-41%) and associated mortality[15–17]. Treatment of VAD-specific and VAD-related infections depends on site, extent, and systemic involvement and is complicated by an inability to remove the device[18,19].

The initial diagnostic approach to cardiovascular infections involves clinical assessment, blood cultures, and basic imaging, including transthoracic and transesophageal echocardiography (TEE). For valvular IE, results from this primary evaluation are combined in a clinical diagnostic algorithm, the modified Duke criteria[20]. Current imaging strategies, however, are not sufficient in all clinical situations. Moreover, the modified Duke criteria have reduced accuracy and have never been validated in the setting of CIED, VAD, and prosthetic material infection. Accurate diagnosis is critical to improve patient outcomes, guide length of antibiotic therapy, and determine the need for surgery or device extraction.

Radionuclide imaging with ^{18}F-fluorodeoxyglucose positron emission tomography-computed tomography (^{18}F-FDG PET/CT, CT portion without contrast) and radiolabeled leukocyte single-photon emission computed tomography (SPECT/CT), in conjunction with cardiac-gated CT angiography (cardiac CTA, in which CT portion is performed with contrast) in select cases, improves assessment of suspected valvular IE, CIED, VAD, and other prosthetic material infection (defined as 'cardiovascular infection' in this document)[21]. These advanced imaging tools can increase diagnostic accuracy, locate sites of involvement, and identify peripheral embolization or other extracardiac manifestations and portal of entry. They also show promise for monitoring treatment response[22,23]. Recognizing their value, guidelines have started incorporating these modalities into the evaluation of cardiovascular infection. The 2015

European Society of Cardiology (ESC) guidelines on infective endocarditis added ^{18}F-FDG PET/CT/radiolabeled leukocyte SPECT/CT imaging as a major criterion in prosthetic valve IE[24]. The European Heart Rhythm Association international consensus document on prevention, diagnosis, and treatment of CIED infections incorporated ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT imaging[25]. A 2018 European Association of Nuclear Medicine (EANM) guideline on nuclear and multimodality imaging in IE provided a literature summary, protocols, and assessment of advantages and limitations of ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT imaging[26]. Updated clinical practice guidelines for the management of endocarditis have recently been published by the ESC in 2023 that provide important advances in diagnostic and therapeutic approaches[27]. However, previous and current guidelines have not fully addressed specific clinical scenarios and appropriate utilization in a systematic manner. Moreover, prior recommendations for ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT have not incorporated input from stakeholder clinical and non-nuclear imaging societies.

Accordingly, the American Society of Nuclear Cardiology (ASNC) assembled a writing group with broad, multispecialty expertise in the clinical management and multimodality imaging evaluation of cardiovascular infection, including representatives from multiple clinical and imaging societies. The goal of this writing group was to develop joint expert consensus recommendations on the use of ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT imaging for the evaluation of cardiovascular infection in the multimodality context. They addressed clinical indications, diagnostic criteria, and a multimodality algorithmic approach to evaluation and management of cardiovascular infection. Evaluation of infection in ports, arteriovenous fistulas, and dialysis catheters, although important, were considered beyond the scope of this document.

This consensus statement provides a concise highlight of the current assessment of cardiovascular infection, addressing the strengths and weaknesses of pertinent imaging modalities. A standardized approach to the incorporation of ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT imaging in the evaluation of cardiovascular infection can improve healthcare quality and outcomes of individuals with this morbid condition. Therefore, the aims of this effort were the following:

1) Assemble a panel of experts from key stakeholder organizations across multiple disciplines to discuss the contemporary role of ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT in cardiovascular infection;
2) Provide a summary of the current clinical criteria and imaging assessment and management of cardiovascular infection;
3) Develop consensus recommendations on diagnostic criteria, clinical indications, and an algorithmic approach incorporating ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT imaging in the setting of multimodality imaging (echocardiography/contrast CT) for cardiovascular infection using the validated modified Delphi technique; and
4) Highlight the application of these consensus recommendations in representative clinical cases.

Assessment of cardiovascular infection

The current assessment of cardiovascular infection involves incorporation of clinical criteria, identification of pathogenic organisms, and findings from an initial imaging approach; however, assessment gaps remain. In the current era, increased device and prosthetic material use create complex considerations that require advanced imaging for optimal decision-making. ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT provide unique insights into the inflammatory process and can be integrated into the multimodality assessment of cardiovascular infection.

Clinical manifestations

The diagnosis of valvular IE derives from a combination of patient-reported symptoms, clinical and radiologic signs, and complications of the disease. Fever, malaise, and weight loss are common symptoms. Rare but highly suggestive signs of IE include Janeway lesions, Osler's nodes, and Roth spots. Splinter hemorrhages, while more common, are not specific for IE. Cardiac conduction abnormalities occur in approximately 15%[28]. Other complications that can occur at any point during the clinical course include heart failure, stroke, septic emboli, metastatic infection, and immune reactions (such as glomerulonephritis).

IE is broadly classified into NVE and prosthetic valve endocarditis (PVE). Diagnosis of IE relies on the identification of the pathogen and visualization of the infected vegetation. Pathogens can be identified by blood cultures or serologies[29]. In cases of prior antibiotic use or difficult-to-culture pathogens, molecular techniques such as polymerase chain reaction of blood and tissue can be performed[30]. The most common causes of IE in high-income countries are *Staphylococcus aureus*, viridans streptococci, and enterococci[6,7]. The mainstay for imaging IE is TEE, which has high sensitivity (85-90%) and specificity (>90%) for native valves[31]. These excellent test characteristics are diminished when assessing for prosthetic valve infection. The decreased sensitivity for detecting vegetations in prosthetic valves highlights the need for adjunct imaging techniques.

The modified Duke criteria codify various microbiologic, imaging, and clinical features of IE into diagnostic categories, which are important for establishing diagnostic clarity in research studies[20]. While these criteria are helpful in the clinical setting, they should not replace careful clinical judgment. A key decision point in the management of IE is whether a patient should undergo surgical treatment. Surgical indications are outlined in the most recent American Association for Thoracic Surgery (AATS), American Heart Association (AHA), and ESC guidelines[24,32–34]. The guiding principles for the medical management of IE include prolonged therapy with bactericidal antibiotics targeted toward the infecting pathogen. Specific recommendations

that take into account the pathogen, antibiotic resistance, and native versus prosthetic valve status are outlined in the AHA and ESC guidelines[24,32,33]. Current clinical criteria for CIED/VAD/prosthetic material infections are not well-defined; this is particularly relevant given their increasing use in clinical practice.

CIED-related infection can involve the generator pocket, intravascular/intracardiac leads, or both. Signs and symptoms of infection depend on which hardware is involved, the responsible pathogen, and timing of presentation[34]. Local pocket involvement ranges from superficial cellulitis to deep infection. The most aggressive infections are more likely to be caused by *S. aureus*[35–37]. Patients with superficial cellulitis usually present with local inflammatory changes, mild purulent drainage, and—in some cases—a small stitch abscess or superficial incisional dehiscence within a few days of a new implant or pocket intervention. Acute deep pocket infections can also present with similar local inflammatory changes within days or weeks of a procedure but can also have more severe manifestations, such as complete wound dehiscence. More commonly, deeper infections can present more than three months to years after a pulse generator change or pocket revision as an indolent infection with subtle signs, such as skin discoloration or adherence of the overlying skin to the generator. These can ultimately progress to device erosion[37]. CIED lead-related bloodstream infections can also present late and are more likely to present with systemic symptoms, such as fever and rigors, and in some cases, sepsis[38]. Gram-negative bacteremia rarely involves CIED systems with a few potential exceptions such as *Pseudomonas aeruginosa* and *Serratia marcescens*[39]. However, many patients, especially with *S. aureus* bacteremia, have CIED system involvement due to the bacterial biofilm created, even when vegetations are not clearly seen[40]. Scenarios where CIED infection is not definitive warrant further testing and close follow-up. CIED infection, whether it is limited to the pocket and/or involves the leads, requires removal of all hardware, intraoperative cultures, and antibiotics for 2-6 weeks depending on the bacteriology and clinical scenario. Delays in device removal and initiation of appropriate antibiotic therapy are associated with one-year morbidity and mortality as high as 25%[41]. If CIED reimplantation is indicated, the contralateral side or a distant site is typically utilized after a minimum of 72 hours of intravenous antibiotics with sterile blood cultures (with or without a temporary pacing system).

Other intrathoracic prosthetic material includes valved tube grafts, such as Bentall-De Bono, other grafts, conduits, and patches. Infection of these materials and VAD infections have no well-defined clinical criteria. These infections can occur early in the post-operative period or as a late complication. Signs and symptoms of VAD infection vary depending on the site and duration of infection. Infections can be silent, involve the local driveline site, or present as sepsis with systemic manifestations[18,19,42]. There may also be overlap in the clinical presentation[43]. Comprehensive evaluation is required due to the heterogeneity of these infections. Treatment of VAD-related infections will depend on the site, extent, and systemic involvement. Patients who present with bacteremia will require initial treatment with broad-spectrum antibiotics to cover both gram-positive and gram-negative organisms[44]. Required surgical interventions may range from isolated debridement to open-chest exploration with wound vacuum closure, or even VAD explantation. These surgical interventions can further increase infection risk. Treatment strategies under these circumstances will vary depending on short- and long-term goals and need a multidisciplinary approach[18,19].

Current strategies based on clinical criteria and an initial imaging approach classify risk and guide therapy. However, in complicated cardiovascular infection, this initial strategy is often insufficient, and advanced imaging is required to provide additional guidance, particularly in patients with multiple implants (i.e., valves and CIED devices).

Role for advanced imaging

Advanced imaging can add important additional information to increase diagnostic accuracy, clarify risk, and optimize treatment. The primary role of ^{18}F-FDG PET/CT in IE is to establish a diagnosis. It can identify patients unlikely to have a cardiovascular origin to infectious etiologies in those with indeterminate echocardiographic findings and identify alternate causes for sepsis. ^{18}F-FDG PET/CT offers complementary whole-body data to clarify infectious source. It can detect distant embolic lesions in up to 35% of patients[45,46]. ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT can assess early infections during the development of periprosthetic complications and can detect extension beyond the valve annulus. ^{18}F-FDG PET/CT can overcome technical limitations in echocardiographic imaging of suspected PVE. Advanced radionuclide imaging can identify the extent of pocket/lead involvement in patients with possible CIED infection. Finally, these tools have shown promise for and may be useful in the future to monitor infection status and response to therapy.

Key surgical and device considerations

The additional information provided by ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT may inform key surgical and device considerations in the appropriate clinical context. Patients who require urgent surgery are not candidates for additional imaging that would cause delay to necessary intervention. Those not in need of urgent intervention may benefit from advanced imaging to define the extent of infection and refine risk stratification. Better characterization of the location and extent of infection could facilitate procedural planning and guide timing[9,32,45]. Identification of high-risk markers may inform patient-centered decision-making and clarify surgical candidacy. CIED or prosthetic material removal typically is recommended when possible. In select cases where the patient is a poor operative candidate, or when removal is not possible, ^{18}F-FDG PET/CT may aid in monitoring infection status, disease recurrence, and response to treatment. This information may be helpful

particularly in patients in whom prosthetic extraction presents challenges[35,47].

Multimodality imaging in cardiovascular infection

Cardiovascular infections, including valvular IE and device and prosthetic material infections comprise complex systemic illness in which involvement of the heart and vascular system is a key component. Imaging is critical to evaluate the extent of cardiovascular involvement and associated complications and to guide management. Echocardiography remains the initial imaging modality assessing cardiovascular infection[31]. CT and radionuclide methods provide additive information[26]. Given the complementary nature of these imaging modalities, this document will focus on the indications to perform these advanced imaging modalities rather than direct comparison of diagnostic accuracy. Radionuclide methods directly image the local inflammatory cellular response to infection, while echocardiography and CT assess structural and functional changes related to infection. Gallium (Ga-67) chloride had a historical role but is no longer routinely used due to limited image quality and sensitivity. The typical radionuclide techniques used in contemporary clinical assessment include ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT (^{99m}Tc, ^{111}In).

Echocardiography

Echocardiography is the standard of care and the most commonly used tool for all types of IE. Echocardiography provides diagnosis, assessment of the severity or valvular or perivalvular lesions, prediction of short- and long-term prognosis and embolic risk, guidance for the management of complications, and assessment of response to therapy[31,48–61].

Echocardiography is almost always the first test performed when IE is suspected. It is a key component of the modified Duke criteria for diagnosis of IE. Its high spatial and temporal resolution allows detection of small vegetations, and its portability allows imaging in all clinical settings, including in patients who are critically ill. In cases of emergency surgery, intraoperative TEE can provide guidance on surgical management. The major echocardiographic criteria for IE, as per the modified Duke criteria, are vegetations and perivalvular lesions (abscesses and pseudoaneurysms)[20,24]. An important additional role of transthoracic echocardiography (TTE) and TEE is to assess underlying valve disease, local consequences of IE, and left- and right-ventricular function. Simultaneous assessment of valve function, including quantification of regurgitation[62,63] or stenosis[64], represents a key advantage of echocardiography for planning treatment of IE.

TTE sensitivity and specificity for detecting NVE ranges from 45 to 87% and 79-98%[54–56]. TEE sensitivity and specificity are generally accepted to be greater than 90% but are confounded by use of TEE as the reference standard in many studies. Three-dimensional (3D) and multiplanar imaging techniques[65] refine the accuracy of echocardiography, particularly in the accurate measurement of vegetation size and identification of perivalvular involvement[66]. Size and location of vegetations also have prognostic significance, particularly for predicting embolism[67].

IE remains difficult to diagnose, especially in prosthetic valves or with implanted cardiac devices. Acoustic shadowing from implanted material may obscure visualization. Accordingly, sensitivity and specificity of TTE for diagnosing PVE is lower (22-65% and 48-98%), but is increased with TEE (83-94% and 87-100%)[51,52,57]. PVE is more likely to be associated with perivalvular extension, and TEE has greater accuracy for detecting these complications than TTE (70% sensitivity and 96% specificity)[53]. IE involving transcatheter aortic valve replacements has a 1.8% per patient-year prevalence and 15-20% of these have perivalvular extension, including in some without vegetations and only rarely with new regurgitation; instead, leaflet thickening and increased gradients may represent the echocardiographic manifestations of IE in these valves[48,68,69].

In the presence of a CIED, echocardiography is indicated to evaluate for lead or valvular vegetations[35]. While TTE has low sensitivity, TEE sensitivity and specificity are high (95-100%) and intracardiac echocardiography shares high diagnostic accuracy[25,58,59,70,71]. Importantly, clots and sterile fibrinous material can often be seen on leads and may not be related to infection[50]. Conversely, failure to see a vegetation on a lead with echocardiography does not rule out lead infection, which demonstrates the need for ancillary imaging modalities. CIED infection may be associated with concomitant valvular endocarditis, which can be evaluated by echocardiography in conjunction with the modified Duke criteria[72,73]. TEE and intracardiac echocardiography are also helpful during lead extraction procedures[49,50].

Echocardiography has limitations in the evaluation of VAD infections[74,75]. Vegetations or abscesses associated with the inflow cannula or the outflow cannula-aortic anastomosis seen on TEE are specific for infection, but the internal surfaces of the device cannot be visualized adequately with echocardiographic techniques, and thus echocardiography is unable to provide a complete evaluation of VAD infection. Congenital heart disease, including repaired shunts and valve lesions, pose unique challenges for diagnosis IE. For example, right ventricular outflow tract conduits may be especially predisposed to endocarditis but are difficult to image with echocardiography[61].

Comprehensive imaging may require off-axis or nonstandard imaging planes to identify small vegetations and fully evaluate struts, frames, and sewing rings. Imaging must also examine for dehiscence, periprosthetic leak, pseudoaneurysms, and surrounding thickening suggestive of abscess. Repeat echocardiography or additional advanced imaging may be required in the setting of negative echocardiography in patients with prosthetic valves, materials and devices; this imaging may also help differentiate infection from late pannus formation, normal endothelialization of CIED hardware, and degenerative calcification of prosthetic material or device-related thrombus[24,76]. Abscess extension, particularly along the aortic root, may be better defined using cardiac CTA.

Echocardiography key points.

- Echocardiography plays a key role in the assessment of cardiovascular infection, including diagnosis, assessment of disease severity, prediction of short- and long-term prognosis, identification of embolic risk, management of complications, and follow-up.
- Echocardiography provides important additional information on concomitant valvular or ventricular dysfunction, allowing for therapeutic decision-making in patients with endocarditis.
- Characteristic echocardiographic findings comprise a major diagnostic criterion for IE.
- Although TEE has higher sensitivity than TTE, both examinations provide independent information and should be systematically performed when cardiovascular infection is suspected.
- The diagnostic value of both TTE and TEE is limited in some subgroups, particularly in patients with cardiac devices, prosthetic valves, or materials, including VADs. A negative echocardiographic study does not rule out infection in these groups, and additional advanced imaging can be considered for early detection of cardiovascular infection. In patients at high risk of IE, repeat TEE at approximately 1 week after a normal index study may be required for diagnosis.

Cardiac computed tomographic angiography

Cardiac CTA has a high spatial resolution and provides useful complimentary information to echocardiography and ^{18}F-FDG PET/CT imaging to diagnose cardiovascular infection and identify complications[46]. Cardiac CTA enables detailed dynamic assessment of prosthetic heart valves in suspected endocarditis; it is a robust imaging method to identify abscess formation; and it is especially well-suited to detect pseudoaneurysms and provide detailed information on pseudoaneurysm shape, size, extent, and anatomical relation to other significant structures. Definite paravalvular lesions by cardiac CTA are listed as a major criterion in the ESC 2015 modified criteria for diagnosis of IE[24]. As an additional benefit, the coronary arteries can be assessed on the same scan, avoiding the need for additional invasive coronary angiography (which increases stroke risk due to dislodged vegetations) prior to surgical intervention[77].

Cardiac CTA image acquisition should cover the entire cardiac cycle by either retrospective electrocardiogram (ECG)-gating or wide-window prospective ECG-triggering with images reconstructed at each 5-10% of the R–R interval[78]. The latter exposes the patients to higher radiation doses, but looping the images from the different reconstruction phases results in cine images that allow assessment of valve leaflet motion and aid identification of vegetations. Images can be reconstructed in any desired imaging plane from the acquired dataset, allowing comprehensive evaluation of infection extent, and facilitating comparison with echocardiographic images.

Cardiac CTA findings in NVE and PVE include: 1) vegetations that present as mobile hypodense masses attached to the valve or cardiac structures; 2) perivalvular extensions, including soft tissue lesions (abscess) or hypodense tissue thickening with rim enhancement (infected collection, often in the aortic root); 3) pseudoaneurysms that are easily spotted as contrast filling cavities; 4) fistulas between adjacent cardiac structures; and 5) valve dehiscence[79,80]. Overall, cardiac CTA provides important anatomical information, particularly to detect perivalvular extension. A recent meta-analysis showed the benefits of this adjunctive imaging. While the sensitivity for valvular vegetations was lower with cardiac CTA compared with TEE (80% versus 91%, $P = 0.019$), this tool identified valvular abscesses with higher accuracy, with sensitivity of 88% vs 74% for TEE, $P = 0.015$[81].

Cardiac CTA is typically combined with ^{18}F-FDG PET/CT to better evaluate IE-related cardiac lesions. Additionally, whole body ^{18}F-FDG PET/CT detects embolic events (e.g., cerebral embolism or splenic/renal abscesses) and/or mycotic aneurysms. The role of CT in CIED infection is limited, as lead vegetations are difficult to detect and the leads and generator cause severe metal artifacts. In patients with suspected VAD infection, cardiac CTA can detect abscesses around the outflow cannula and driveline. The pump itself causes severe artifacts, prohibiting assessment.

Cardiac computed tomographic angiography key points.

- Cardiac CTA provides important complementary information to the valvular function obtained by echocardiography and the metabolic data obtained by ^{18}F-FDG PET/CT and/or radiolabeled leukocyte SPECT/CT.
- Retrospective or wide-window prospective ECG-gated acquisition of the entire cardiac cycle is preferred for dynamic valve assessment by cardiac CTA.
- Concomitant coronary artery assessment on the same cardiac CTA scan can prevent the need for preoperative invasive coronary angiography.
- Cardiac CTA may be combined with ^{18}F-FDG PET/CT to assess IE-related cardiac lesions and systemic complications.
- Definite paravalvular lesions detected by cardiac CTA are included as a major criterion for IE in the ESC 2015 guidelines[24].

Radiolabeled leukocyte SPECT/CT

Radiolabeled leukocyte SPECT/CT is a well-established technique to image infectious processes. It has been utilized in the evaluation of cardiovascular infection, especially for CIED and early post-operative infections, the time period in which ^{18}F-FDG PET/CT has limited specificity.

This test is performed without specific patient preparation and can take up to 24 hours to complete. Leukocytes are isolated from a 30-50 mL autologous blood sample and radiolabeled with either ^{99m}Tc-HMPAO or ^{111}In-oxine followed by intravenous reinjection under sterile conditions[82,83]. ^{99m}Tc-HMPAO is preferred due to superior resolution on SPECT/CT imaging. Images are usually acquired 4- and 24-hours post-

injection. They consist of whole-body planar imaging followed by SPECT/CT acquisitions focused on the region of interest. The detection of radiolabeled leukocyte accumulation on 4-hours imaging with increasing contrast-to-noise ratio in the same region on 24-hours imaging is highly specific for material infection and/or the presence of an abscess[84]. The region of radiolabeled leukocyte accumulation is localized best through SPECT/CT acquisition, using both CT attenuation and non-CT attenuation corrected SPECT images.

Radiolabeled leukocyte SPECT/CT is used less widely due to limited sensitivity to detect IE, particularly in suspected NVE. However, it has high specificity for infection and may be helpful to differentiate infective from inflammatory processes in patients with equivocal ^{18}F-FDG PET/CT findings. This high specificity has been validated in patients with a suspicion of NVE or PVE[85–87], as well as in CIED[88,89], VAD[90], and vascular graft infection[91]. The presence of a signal on radiolabeled leukocyte SPECT/CT is classified as a major criterion for IE in patients with a suspicion of PVE and an additive tool in possible CIED infection (ESC guidelines for IE)[24]. Typically, unlike with ^{18}F-FDG PET/CT, there is no background signal in the myocardium nor artifacts related to the presence of prosthetic material. Radiolabeled leukocyte SPECT/CT provides the ability to detect systemic embolization phenomena and identify extra-cardiac sources of infection with whole-body imaging.

Radiolabeled leukocyte SPECT/CT has low spatial resolution and low signal intensity at 24-hours post-injection, limiting detection of small infective foci[92]. Of note, radiolabeled leukocyte SPECT/CT has reduced sensitivity in non-pyogenic and chronic infections (as with *Coxiella* and *Tropheryma whipplei*). Additionally, radiolabeled leukocyte SPECT/CT may require a two-day imaging protocol with relatively long acquisition times. Recommendations in this paper are based on SPECT/CT hybrid imaging and not planar or SPECT images alone.

Radiolabeled leukocyte SPECT/CT key points.

- Radiolabeled leukocyte SPECT/CT scanning is a well-established technique to image infectious processes and requires no specific patient preparation.
- Radiolabeled leukocyte SPECT/CT is used to image IE sustained by pyogenic microorganisms, but has limited sensitivity, particularly for lesions less than 1 cm and in non-pyogenic infections.
- It has high specificity to identify cardiovascular infection, particularly in the presence of suspected or known CIED infection or with an equivocal PET early after surgery.
- Radiolabeled leukocyte SPECT/CT signal is included as a major criterion in the ESC 2015 guidelines for IE in patients with suspected PVE and as an additive tool in possible CIED infection[24].

^{18}F-FDG PET/CT

^{18}F-FDG PET/CT is a sensitive marker for inflammation and infection, making it an attractive non-invasive tool for the investigation of cardiovascular infection. ^{18}F-FDG is a glucose analog that is taken up in metabolically active inflammatory cells, which express high levels of the glucose transporters, Glut-1 and Glut-3[93]. ^{18}F-FDG PET/CT has long been used as an imaging marker for inflammation and infection, including in applications such as infected musculoskeletal prostheses and identifying infectious source in fever of unknown origin (FUO). Cardiovascular utilization was limited primarily due to challenges in differentiating pathologic from normal physiologic myocardial uptake. Development of methods to suppress physiologic uptake have increased cardiovascular application for inflammatory conditions, such as sarcoidosis and in cardiovascular infection[94]. Accumulating evidence has increased recognition of the value of ^{18}F-FDG PET/CT in defining diagnosis, refining prognosis, and guiding management of patients with a suspicion of cardiovascular infection. Consequently, utilization of ^{18}F-FDG PET/CT for this indication over the past decade is increasingly considered. Moreover, in this context, Centers for Medicare & Medicaid Services (CMS) retired a non-coverage decision for ^{18}F-FDG PET for infection, and inflammation imaging and coverage determinations are now made locally. These factors have led to a substantial interest in using ^{18}F-FDG PET/CT in imaging infection, including for cardiovascular applications.

As ^{18}F-FDG normally accumulates in myocardial tissue, PET/CT imaging for cardiac infection requires a special patient preparation consisting of a high-fat, low-carbohydrate ketogenic diet typically starting 24 hours prior to the study followed by a 12-hours fast[95]. Recent studies report better test performance in the setting of higher compliance with recommended pre-scan diet preparation[96]. Myocardial suppression improves diagnostic accuracy, particularly for IE assessment, but can be withheld when urgent imaging is required. On hybrid PET/CT imaging, it is important to confirm ^{18}F-FDG uptake on non-attenuation corrected images in the setting of prosthetic valves, CIED hardware, or other prosthetic material because the presence of material on low-dose CT may lead to overcorrection of the PET images. There is growing evidence to support the use of combined ^{18}F-FDG PET/CT with cardiac CTA to improve visualization of structural IE-related lesions (i.e. pseudoaneurysms or fistulas), resulting in higher diagnostic accuracy[46]. In addition, both (ECG-gated) cardiac and whole-body images are obtained[97].

^{18}F-FDG PET/CT can provide important additive information to a cardiovascular infection workup. Applications of ^{18}F-FDG PET/CT in this context are provided in Table 1. ^{18}F-FDG PET/CT can provide a comprehensive evaluation of infectious involvement. While structural imaging can detect tissue remodeling, ^{18}F-FDG PET/CT can assess the degree and extent of inflammation in infected cardiac lesions. Whole-body images can identify portal of entry and reveal embolic phenomena and mycotic aneurysms, except in the brain owing to the high physiologic ^{18}F-FDG signal in this organ[98]. Serial ^{18}F-FDG PET/CT imaging may have a role for monitoring disease course and response to therapy. The accuracy of ^{18}F-FDG PET/CT for cardiovascular infection has

Table 1 Applications of ^{18}F-FDG PET/CT for evaluation of suspected cardiovascular infection.

- Define extent of infection (e.g., involvement of the ascending aortic root)
- Localize infection (particularly with multiple devices/prostheses)
- Identify infection in areas not or suboptimally imaged by TEE (prosthetic material, conduits)
- Detect abscess
- Detect infectious complications
- Identify embolic phenomena
- Identify portal of entry (to address other areas of infection)
- Guide risk assessment
- Detect metabolically active lymph nodes
- Exclude endocarditis as a source of fever/symptoms, particularly in suspected prosthetic valve endocarditis, and is less reliable for possible native valve endocarditis or CIED-related infection

been closely examined in more than 40 original articles and 6 meta-analyses over the past decade. A summary of this extensive literature is provided in Table 2. For PVE, this summary reveals a high sensitivity, range 73-80% and specificity, range 71-91%. In NVE, there is a similarly high specificity, range 78-99%, but sensitivity is lower, ranging 14-77%, with sensitivity low, in particular, for detection of small vegetations. ^{18}F-FDG PET/CT has high sensitivity for LVAD infection, range 87-95%.

Application of ^{18}F-FDG PET/CT in PVE is well-established, and there is growing experience in suspected CIED and VAD infection. The diagnostic accuracy is affected by the timing of imaging in relation to device implantation and the specific device component under assessment (e.g., driveline, pocket, lead). The duration post-surgery during which uptake is seen has not been definitively determined. ^{18}F-FDG PET/CT is limited in assessing cerebral complications, for which brain MRI is often used. ^{18}F-FDG PET/CT has reduced specificity in the context of implantation of certain valve models or with use of specific bioadhesives. Novel quantitative metrics, such as the valve uptake index (standardized uptake value [(SUV_{max} – SUV_{mean})/SUV_{max}), may help improve the diagnostic accuracy of ^{18}F-FDG PET/CT for PVE, particularly in the early post-operative period[99]. Added to these factors, study heterogeneity in inclusion/exclusion criteria and applied diagnostic criteria affect test characteristics.

^{18}F-FDG PET/CT key points.

- ^{18}F-FDG PET/CT requires specific patient dietary preparation to optimize diagnostic accuracy in assessment of certain suspected cardiovascular infection.
- ^{18}F-FDG PET/CT has an important additive role to echocardiography and cardiac CTA assessment in some patients with suspected cardiovascular infection.
- This modality has higher diagnostic accuracy in suspected PVE and CIED infection compared to use in suspected NVE.
- ^{18}F-FDG PET/CT can identify systemic embolic phenomenon in many cases.
- ^{18}F-FDG PET/CT can potentially identify the portal of entry and alternative causes for sepsis.

Methods

The methodology of the ASNC I^2 series has been detailed extensively and published previously[100]. The clinical rating portion of this document involves rigorous procedures adapted from the original RAND/UCLA Appropriateness Method and prior appropriateness documents addressing radionuclide imaging and cardiovascular disease[101–103]. A clinical expert rating panel was assembled with broad multidisciplinary representation. This group conducted a thorough literature review, which was then employed during creation of consensus diagnostic criteria for cardiovascular infection, an algorithmic approach to diagnosis, and clinical indications for radionuclide imaging. These were rated using a common appropriateness scale over multiple rounds employing a rigorous modified Delphi technique. It is important to note that the 2023 ESC Guidelines for the management of endocarditis were published after the expert panel performed their ratings and constructed the document[27].

Expert panel creation and literature review

A multisocietal clinical expert rating panel was assembled, including 15 members as recommended by the RAND/UCLA Appropriateness Method User's Manual[103]. The panel included substantial representation by clinicians across disciplines caring for the patient population under study, including general cardiology, infectious disease, cardiothoracic surgery, and electrophysiology. In addition, imagers with expertise in radionuclide imaging from multiple societies were incorporated to provide imaging and technical expertise. Panel members were nominated by multiple participating societies (ASNC, AATS, American College of Cardiology [ACC], AHA, American Society of Echocardiography [ASE], EANM, Heart Rhythm Society [HRS], Infectious Disease Society of America [IDSA], Society of Cardiovascular Computed Tomography [SCCT], Society of Nuclear Medicine and Molecular Imaging [SNMMI], and The Society of Thoracic Surgeons [STS]), work in varied practice settings, and were recruited from diverse geographical locations. The writing group reviewed and approved the clinical indications, diagnostic criteria and algorithm, and final document. The imaging experts created the high-yield concise imaging modality summaries.

A thorough literature review was performed to guide clinical indication development and rating, starting with a broad canvas using search terms, including "endocarditis", "valve infection", "lead infection", "pacemaker infection", "pocket infection", "cardiac device infection", "ICD infection", "LVAD infection", "VAD infection", "prosthetic valve infection", "pacemaker", "ICD", "LVAD", "VAD", and "prosthetic valve" combined with "positron-emission tomography/PET", "radionuclide imaging", "leukocyte scintigraphy", "fluorodeoxyglucose", and "single-photon emission computed tomography [SPECT]". Individual articles were evaluated to identify relevant material. These materials were available for review by the expert panel, and all members reviewed a summary prior to their creation of the consensus material and indication rating.

Table 2 Summary of key meta-analyses and large studies addressing accuracy of ^{18}F-FDG PET/CT for cardiovascular infection[120,137,141].*

Author Year	Indication	Studies (n)	Patients (n)	Sensitivity	Specificity
Wang 2020[120]	NVE	4	385	0.31	0.98
Albano 2021[142]	NVE	12	600	0.31	0.82
Kamani 2020[143]	NVE	7	351	0.36	0.99
Gomes 2017[144]	NVE	7		0.14	
Mahmood 2019[141]	NVE + PVE	13	537	0.77	0.78
Wang 2020[120]	PVE	15	967	0.86	0.84
Mahmood 2019[141]	PVE	8	227	0.80	0.73
Swart 2018[133]	PVE	1	237	0.74	0.91
Gomes 2017[144]	PVE	8		0.73–1.0	0.71–1.0
The reference standard for PVE/NVE varied between determination by Modified Duke-Li criteria, multidisciplinary endocarditis team, follow-up, histology, or a combination of these.					
Wang 2020[120]	CIED Endocarditis	9	297	0.72	0.83
Mahmood 2019[141]	CIED Infection	14	492	0.83	0.89
Mahmood 2019[141]	CIED Pocket Infection	3		0.96	0.97
Mahmood 2019[141]	CIED Lead Infection	7		0.76	0.83
Juneau 2017[137]	CIED Infection	11	340	0.87	0.94
Gomes 2017[144] **	CIED Infection	9		0.8–0.89	0.86–1.0
Gomes 2017[144]	CIED Endocarditis	1		0.31	0.63
Gomes 2017[144]	CIED Lead Infection			0.24–1.0	0.79–1.0
Gomes 2017[144]	CIED Pocket Infection			0.87–1.0	0.93–1.0
The reference standard for CIED infection varied between culture, follow-up, or laboratory/clinical data.					
Ten Hove 2021[145]	LVAD Infection	8	230	0.95	0.91
Tam 2020[146]	LVAD Infection	4	119	0.92	0.83
Sommerlath Sohns 2020[147] †	LVAD driveline Infection	1	57	0.87	0.59
The reference standard for LVAD infection included INTERMACS or ISHLT criteria, clinical data, culture, follow-up, or histology.					

CIED = cardiovascular implantable electronic device; INTERMACS=Interagency Registry for Mechanical Circulatory Support criteria, ISHLT=International Society of Heart and Lung Transplantation criteria, LVAD = left ventricular assist device; NVE = native valve endocarditis; PVE = prosthetic valve endocarditis.
*There is no meta-analysis or large studies available addressing prosthetic material infection.
**This study is not a meta-analysis but is the largest single-site study on LVAD infection.
†Number of patients not provided subdivided by type of infection.

Diagnostic criteria and algorithm development

Current diagnostic criteria and algorithms for diagnosis of cardiovascular infection are based on the modified Duke criteria with the introductory inclusion of PET and CT in the 2015 ESC guidelines and further supported in the 2023 ESC guidelines[24,27]. This document builds on established guidance by addressing specific imaging features to support diagnosis and incorporates contemporary advances since these documents were published. The expert panel created consensus diagnostic criteria and an algorithmic approach to diagnosis that incorporate clinical, histologic, biomarker, and multimodality imaging features. These recommendations synthesize available evidence, add expert opinion where there is insufficient data, and incorporate systemic diagnosis while focusing on cardiac involvement.

Clinical indication derivation and rating

Full details on the methodology used for the derivation and rating of clinical indications are provided in the published ASNC I^2 Methodology document[100]. In brief, the expert rating panel created broad clinical scenarios representing key clinical care areas in which advanced imaging could be considered. For each scenario, they identified individual clinical indications encompassing situations in which radionuclide imaging may be considered in the multimodality imaging context, including for diagnosis, risk stratification, and management based on literature available at the time of rating.

Both ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT were evaluated. The authors acknowledge that the latter has reduced sensitivity for inflammation and is not the first-line recommended technique when cardiovascular infection is suspected. It may be necessary in those institutions in which only radiolabeled leucocyte SPECT/CT is available and preferred in the early post-operative setting, when a high degree of specificity is needed. The raters rated both radionuclide techniques independently, but an assumption of the document is that ^{18}F-FDG PET/CT would be the preferred modality if both are available, unless specifically noted.

Modified Delphi technique

The expert rating panel rated the appropriateness of each clinical indication for both ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT using a modified Delphi technique as used in multiple appropriate-use documents[101,102,104–106]. Indication rating occurred over three rounds: an individual rating after literature review followed by two rounds held via recorded video conference. A quorum of greater than 70% was achieved for all meetings, with absent members

reviewing the complete recording prior to rating. Some small modifications of the indications were made during the rating sessions with complete re-rating by all panel members where necessary. Agreement was set according to the BIOMED Concerted Action on Appropriateness Methods for a 15-member panel as less than 5 panel members rating outside the consensus appropriateness category[101,102,104–106]. Indications without agreement were categorized as May Be Appropriate.

Clinical indication rating

Appropriateness rating of the clinical indications followed a standardized system as adopted by the ASNC I^2 series[100] and adapted from other documents addressing appropriateness[102,104,105,107] with the following guideline:

> *An appropriate imaging study is one in which the expected incremental information, combined with clinical judgment, exceeds the expected negative consequences by a sufficiently wide margin for a specific indication that the procedure is generally considered acceptable care and a reasonable approach for the indication.*

A linear scale of appropriateness was used (1-9), with scores divided into three categories: Appropriate (A), May Be Appropriate (M), or Rarely Appropriate (R). The definitions listed below are adapted from prior appropriate use documents and were provided to the expert rating panel prior to the start of the rating process[101,102,108].

Appropriate (score 7-9). An indication scored in the Appropriate range (score 7-9) signifies that the imaging procedure is judged to be an appropriate option for management of patients in the population addressed in the document for this indication. The benefits of imaging for this clinical indication generally outweigh the risks. The imaging procedure should be considered an effective option for individual care plans but may not always be necessary, preferred, or chosen based on physician judgment and patient-specific preferences. The procedure is judged to be generally acceptable and is generally reasonable for the assessed clinical indication.

May Be Appropriate (score 4-6). An indication scored in the May Be Appropriate range (score 4-6) signifies that the imaging procedure assessed is, at times, an appropriate option for management of patients in the population addressed in the document for this indication. The reduced strength of recommendation is due to variable evidence or agreement regarding the risk-benefit ratio, potential benefit based on practice experience in the absence of evidence, and/or variability in the population. The effectiveness of this imaging procedure for a patient's individual care plan must be determined by the patient's physician in consultation with the patient based on additional clinical variables and judgment and incorporating patient preferences. The procedure may be acceptable and may be reasonable for the assessed clinical indication. Of note, a May Be Appropriate categorization may also indicate that further research and/or patient information is needed to classify the indication definitively.

Rarely Appropriate (score 1-3). An indication scored in the Rarely Appropriate range (score 1-3) signifies that the imaging procedure is judged rarely to be an appropriate option for management of patients for this clinical indication due to a lack of a clear benefit/risk advantage. Physician judgment and patient-specific preferences should be considered, but the imaging procedure should rarely be exercised as an effective option in individual care plans for this indication. Moreover, exceptions should have documentation of the clinical reasons for proceeding with this care option. The procedure is not generally acceptable and is not generally reasonable for the assessed clinical indication.

This score division is somewhat arbitrary, and raters were instructed to consider the numeric range a continuum. Raters were also advised to rate based on best available evidence incorporating guidelines and key references where possible and acknowledging some variability in patient factors and local practice patterns[106].

Assumptions

The following assumptions have been adopted for the ASNC I^2 series as adapted from prior appropriate use documents and methodology recommendations[100,101,104,106,109,110]. They were provided to the expert panel prior to the start of the rating process. These assumptions minimize variability in competence, test quality, and other concerns separate from the clinical indication for the rating process.

- All imaging studies will be assumed to be available locally and to be performed in accredited imaging laboratories in accordance with published criteria for quality cardiac diagnostic testing using state-of-the-art, certified imaging equipment.
- All imaging will be assumed to be performed according to the standard of care as defined by the peer-reviewed medical literature.
- All interpreting physicians will be assumed to be qualified and certified to supervise the imaging procedure and appropriately report the findings.
- In clinical scenarios, the clinical status listed will be assumed to be valid as stated (asymptomatic patients are truly asymptomatic) and no extenuating circumstances will be taken into consideration (patient willingness to receive treatment, clinical stability) unless specifically noted.
- Appropriateness will be rated independently of the appropriateness of any prior diagnostic imaging that may have been performed in the clinical indication/scenario.
- Imaging indicated for surveillance to assess disease progression or response to therapy is assumed to be performed solely because the indicated time period elapsed rather than due to any change in clinical circumstances.
- Test appropriateness will be considered under the assumption that many patients will have been on appropriate antibiotics for some time prior to testing, potentially affecting imaging sensitivity.

- Cost of the imaging procedures will not be considered in accordance with recommended appropriateness scoring methods[101,106]. These analyses focus purely on whether benefits outweigh risks and do not imply that the imaging procedure must be done for all patients. Cost is recognized to be an important issue from a coverage policy and payment perspective and is frequently incorporated into clinical practice; however, it is not recommended for appropriateness analyses. Moreover, expert physician appropriateness ratings have been shown to agree well with cost-effectiveness models[111,112].

Definitions

The following definitions clarify terms used in the consensus criteria, algorithms, and clinical indications. They rely on prior published guidelines and key papers where possible.

1. **CIED**: Cardiovascular implantable electronic device, most of which have leads connecting a generator to cardiac tissue[35]. Examples include implantable cardioverter defibrillators (ICD), permanent pacemakers, cardiac resynchronization therapy devices, abandoned CIED/transvenous leads, as well as pacing leads and defibrillation patches and coils that reside on the epicardial surface but are tunneled to the CIED pocket.
2. **Complicated Valvular Endocarditis**: Complicated valvular endocarditis includes invasive infection with peri-valvular/peri-prosthetic extension, systemic embolism/high embolic risk, uncontrolled infection, or heart failure[24].
3. **Deep versus Superficial Soft-Tissue Device Pocket Infection**: Superficial infections are limited to the skin and subcutaneous layers of the incision and have not spread to the underlying CIED hardware. Deep soft-tissue pocket infections encompass all other situations, including involvement of the fascia, muscle, and CIED hardware within the pocket[35]. Deep pocket infections can also present with evidence of systemic infection involving CIED leads and endocardial tissues.
4. **Early Post-Operative Period:** For this document, the early post-operative period was defined as 3 months, the time during which ^{18}F-FDG PET/CT has reduced specificity.
5. **Fever of Unknown Origin (FUO):** Temperature greater than 38.3 °C on several occasions during a period lasting longer than 3 weeks with a diagnosis remaining uncertain after 1 week of inpatient evaluation[113].
6. **HACEK Organisms**: The Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella, and Kingella (HACEK) organisms refer to the following gram-negative bacteria that can cause cardiovascular infection: Haemophilus species, *Aggregatibacter actinomycetemcomitans*, Cardiobacterium hominus, *Eikenella corrodens*, and *Kingella kingae*[114].
7. **Inflammatory Markers:** Inflammatory markers associated with cardiovascular infection include C-reactive protein, erythrocyte sedimentation rate, and leukocyte count[24,115].
8. **VAD Infection Location:** VAD infections can be separated into three distinct locations as defined by the International Society for Heart and Lung Transplantation: (1) pump and inflow/outflow cannula; (2) pocket; or (3) involving the percutaneous driveline[116].
9. **Native versus Prosthetic Valve:** Native valves include a patient's original valvular tissue. Prosthetic valves include mechanical and bioprosthetic valves (surgically placed or transcatheter), as well as prosthetic materials, such as clips and rings.
10. **Persistent Bacteremia/Fungemia/Sepsis:** There is no uniform definition for persistent bacteremia/fungemia/sepsis. For this document, persistent infection was defined as positive blood cultures for two or more days despite appropriate therapy with antibiotics or antifungal agents and removal of suspicious removable sources[44].
11. **Prosthetic Material**: For the purposes of this document, prosthetic material is comprised of grafts, conduits, and patches. Although prosthetic valves and CIEDs are also prosthetic material, they are discussed separately in this document.
12. **Sepsis**: The guidelines recognize sepsis as life-threatening organ dysfunction secondary to a dysregulated host response to infection consistent with the Sepsis-3 consensus definition[37].

Results

Diagnostic features and an algorithmic approach to evaluation of cardiovascular infection

Diagnostic criteria for IE are well-established[20]. The 2015 ESC guidelines expanded these to include advanced imaging with cardiac CTA, ^{18}F-FDG PET/CT, and radiolabeled leukocyte SPECT/CT[24]. This document provides increased granularity and highlights complementary imaging features of ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT. It also expands the scope of use of these advanced imaging techniques from NVE and PVE to CIED, VAD, and prosthetic material infection. Table 3 provides recommendations on diagnostic features for ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT in the evaluation of cardiovascular infection. Consensus recommended algorithmic approaches for the evaluation of cardiovascular infection are provided in Figures 1 and 2. Advanced imaging can help improve diagnosis, refine risk stratification, guide surgical decision-making, and optimize clinical management. Figure 1 addresses NVE, PVE, and prosthetic material infection. Figure 2 provides an algorithmic diagnostic approach for suspected CIED infection.

Indications for ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT

The appropriate utilization ratings for ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT are documented in Table 4 for suspected NVE and PVE, and in Tables 5–7 for suspected infection of CIEDs, prosthetic material, and VADs, respectively. This advanced imaging can help solidify diagnosis, clarify surgical decision-making, and refine

Table 3 Diagnostic considerations and suggestive patterns for ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT in suspected cardiovascular infection.

General Comments		
• Unless specified the recommendations apply to both ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT. Features specific to either one of the modalities are listed in a separate row • ^{18}F-FDG PET/CT: Use with caution early (approx. 3 months) after (complicated) surgical intervention • Radiolabeled Leukocyte SPECT/CT: Use limited to pyogenic infections; limited sensitivity for small vegetations		
Valvular	Native Valvular	• Provides supportive information • Insufficient data to recommend current role for valvular assessment
	Prosthetic Valvular	• Focal/multifocal or diffuse heterogeneous, intense intravalvular (in the leaflets), valvular (following the supporting structure of the valve), or peri-valvular tracer uptake persisting on NAC images*,** [148] • Focal tracer uptake corresponding to an IE-related lesion visualized on cardiac CTA or other imaging increases likelihood of a true positive† • Diffuse mild homogeneous tracer uptake is often found in prostheses and has reduced specificity as it can represent a normal, non-infective pattern • ^{18}F-FDG uptake in the presence of surgical adhesives may have reduced specificity
	Peripheral Findings	• Focal tracer uptake in organs without typical physiological uptake may be consistent with septic embolism, mycotic aneurysm, or a potential portal of entry. Corresponding abnormalities on additional imaging can increase diagnostic certainty • Photopenic areas in organs with physiologic radiolabeled leukocyte or ^{18}F-FDG uptake requires further assessment to exclude septic embolism presence • Focal ^{18}F-FDG uptake may identify central nervous system involvement, but contrast-enhanced CT or MRI are required to rule-out infection in this location
CIED	Lead	• Focal/multifocal or diffuse heterogeneous, or linear intense tracer uptake along/adjacent to the leads persisting on NAC images • Uptake corresponding to a suspected area of lead infection (i.e., mobile elements on echocardiography) increases likelihood of a true positive • Isolated uptake at the point of lead passage into the subclavian vein has reduced specificity [149]
	Pocket	• Focal/multifocal or diffuse heterogeneous, intense tracer uptake in the region of the generator pocket persisting on NAC images • Delineation of superficial versus deep involvement should be included in the assessment
	Peripheral Findings	• Focal/multifocal or diffuse heterogeneous, intense intravalvular (in the leaflets), valvular (following the supporting structure of the valve) or peri-valvular tracer uptake persisting on NAC images consistent with associated infective endocarditis (often involving the native tricuspid or implanted prosthetic valves) • Linear pericardial uptake consistent with associated pericarditis • Focal tracer uptake in organs of non-physiological uptake is consistent with septic embolism (particularly multiple septic pulmonary emboli), portal of entry, or mycotic aneurysm (unusual in right-sided IE) • Photopenic areas in organs with physiologic radiolabeled leukocyte uptake (i.e., spleen and spine) require further assessment to exclude septic embolism presence
LVAD	Driveline	• Focal/multifocal or diffuse heterogeneous, linear intense tracer uptake adjacent to the driveline persisting on NAC images [140,150–154]
	Pump/Cannula	• Focal/multifocal or diffuse heterogeneous, intense tracer uptake persisting on NAC images with associated infiltration around the pump present on non-enhanced CT [149] • Diffuse mild homogeneous tracer uptake is often found in prostheses and has reduced specificity as it can represent a normal, non-infective pattern
Prosthetic Material	Graft Materials	• Focal/multifocal or diffuse heterogeneous tracer uptake with intensity equal to or greater than liver or equal to spleen is often associated with abnormalities on the corresponding non-enhanced CT • ^{18}F-FDG uptake in regional lymph nodes may increase specificity [155]
	Peripheral Findings	• Focal tracer uptake in organs of non-physiological uptake is consistent with associated infections, septic embolism, mycotic aneurysm, or the portal of entry

Cardiac CTA = cardiac-gated computed tomographic angiography; FDG = fluorodeoxyglucose; MRI = magnetic resonance imaging; NAC = non-attenuation corrected; WBC=Radiolabeled leukocyte.

*Data on use of NAC images in radiolabeled leukocyte scintigraphy is limited with concern about possible decreased sensitivity due to lower resolution and more substantial attenuation.

**Time post-implantation is less important than uptake pattern for risk of false-positive results [148,156].

†Suggestive cardiac CTA findings include diffuse valvular thickening without vegetation; low/intermediate-attenuation mobile soft-tissue lesions attached to valves, endocardium, or prosthetic material (vegetation); leaflet tissue defect observed in >1 dimensional view (perforation); soft-tissue thickening around a valve/prosthesis or graft (abscess); contrast-filled sacculation arising from a cardiac/vascular structure (pseudoaneurysm).

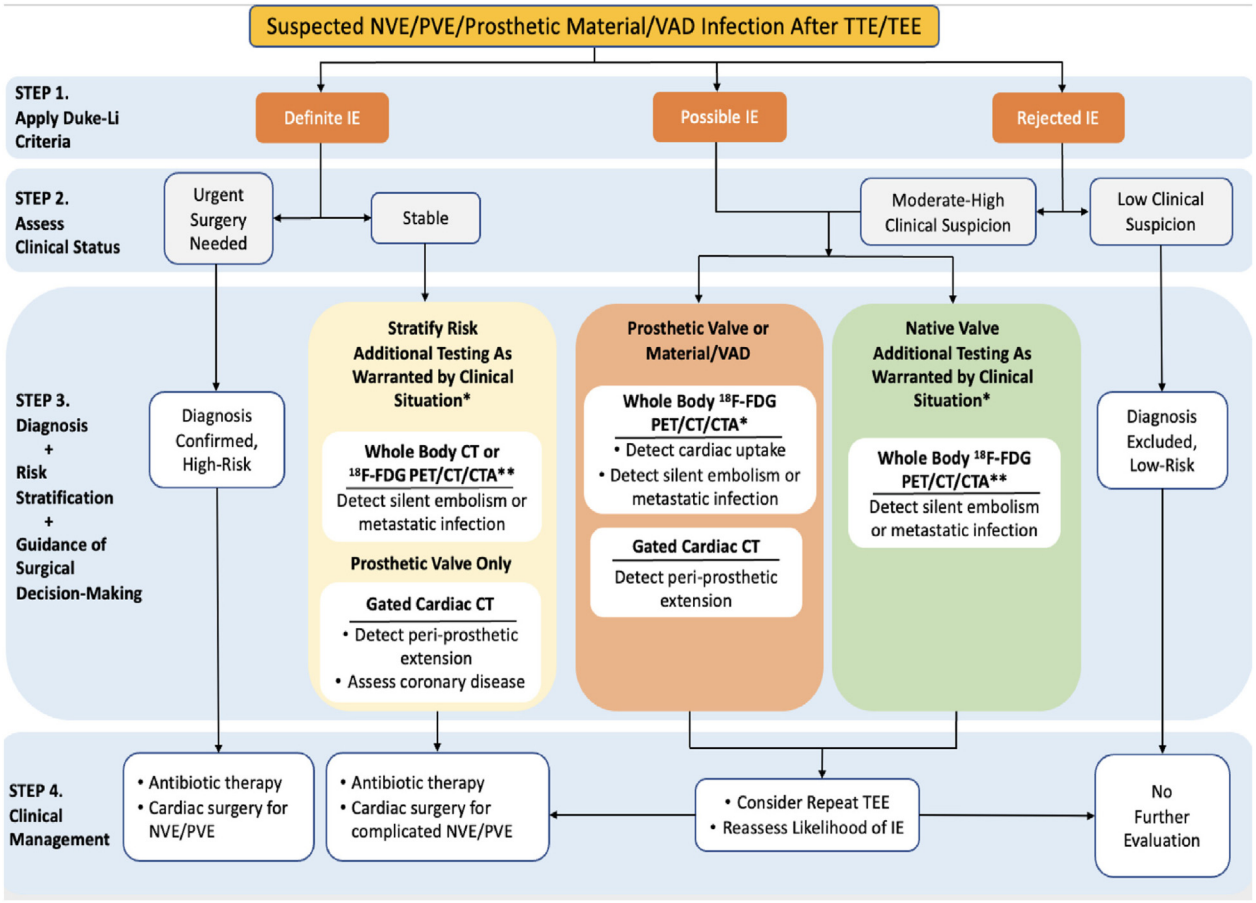

Figure 1

Diagnostic Algorithm Flowchart for Suspected Native or Prosthetic Valve Endocarditis or Prosthetic Material/VAD Infection. A consensus algorithmic approach is provided for patients with suspected NVE, PVE, or prosthetic material infection incorporating the Duke-Li criteria, clinical status, and varied diagnostic and risk stratification approaches to affect clinical management. *Clinical situations warranting consideration of further testing include signs, symptoms, and/or other imaging suggest perivalvular/periprosthetic complications or extracardiac manifestations. **Radiolabeled leukocyte SPECT/CT may be substituted in specific circumstances or if PET/CT is not available. CT = computed tomography; Cardiac CTA = cardiac-gated computed tomographic angiography; IE = infective endocarditis; NVE = native valve endocarditis; PET = positron emission tomography; PVE = prosthetic valve endocarditis.

antibiotic adjustment and duration. In some clinical situations other types of imaging may be contraindicated or may be preferred (e.g., brain MRI in suspected PVE in patients with neurologic signs/symptoms). Moreover, due to the complexity of clinical care, the more common clinical situations were addressed, but all scenarios could not be covered. Discussion and key considerations for clinical indications are provided below.

Native valve endocarditis

^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT can be useful for the diagnosis and management of NVE in select clinical scenarios, particularly in conjunction with cardiac CTA[117]. In specific cases of NVE with possible IE or IE rejected by modified Duke criteria but high clinical suspicion, ^{18}F-FDG PET/CT is considered Appropriate when echocardiography is negative or equivocal for the finding of interest. For example, ^{18}F-FDG PET/CT is considered Appropriate in the setting of positive blood cultures for a gram-positive or typical gram-negative organism (such as HACEK group), a high clinical suspicion for IE (e.g., with persistent bacteremia), and with negative TEE[118]. Similarly, ^{18}F-FDG PET/CT is considered an Appropriate diagnostic test if the TEE is inconclusive or equivocal for the presence of a vegetation or perivalvular abscess[119,120]. Conversely, in a clinical scenario where a patient is found to have a mobile mass (>5 mm) on echocardiography but a negative microbiological workup, ^{18}F-FDG PET/CT is Appropriate, as it may be useful to distinguish NVE from a mass due to a non-infectious etiology.

^{18}F-FDG PET/CT is considered less useful in patients with fungemia or non-HACEK gram-negative bacteria who have a negative TEE[121–123]. Patients who have persistent bacteremia and fungemia need to be considered on an individual, case-by-case basis, and ^{18}F-FDG PET/CT May Be Appropriate to assist diagnosis. Similarly, ^{18}F-FDG PET/CT May Be Appropriate for patients with FUO who have a negative initial evaluation[94,124–126]. Because ^{18}F-FDG PET/CT can detect foci of infection outside of the heart, it can also be useful for detecting extra-cardiac foci and the infection port of entry (including infection of extracardiac hardware)[127]. As

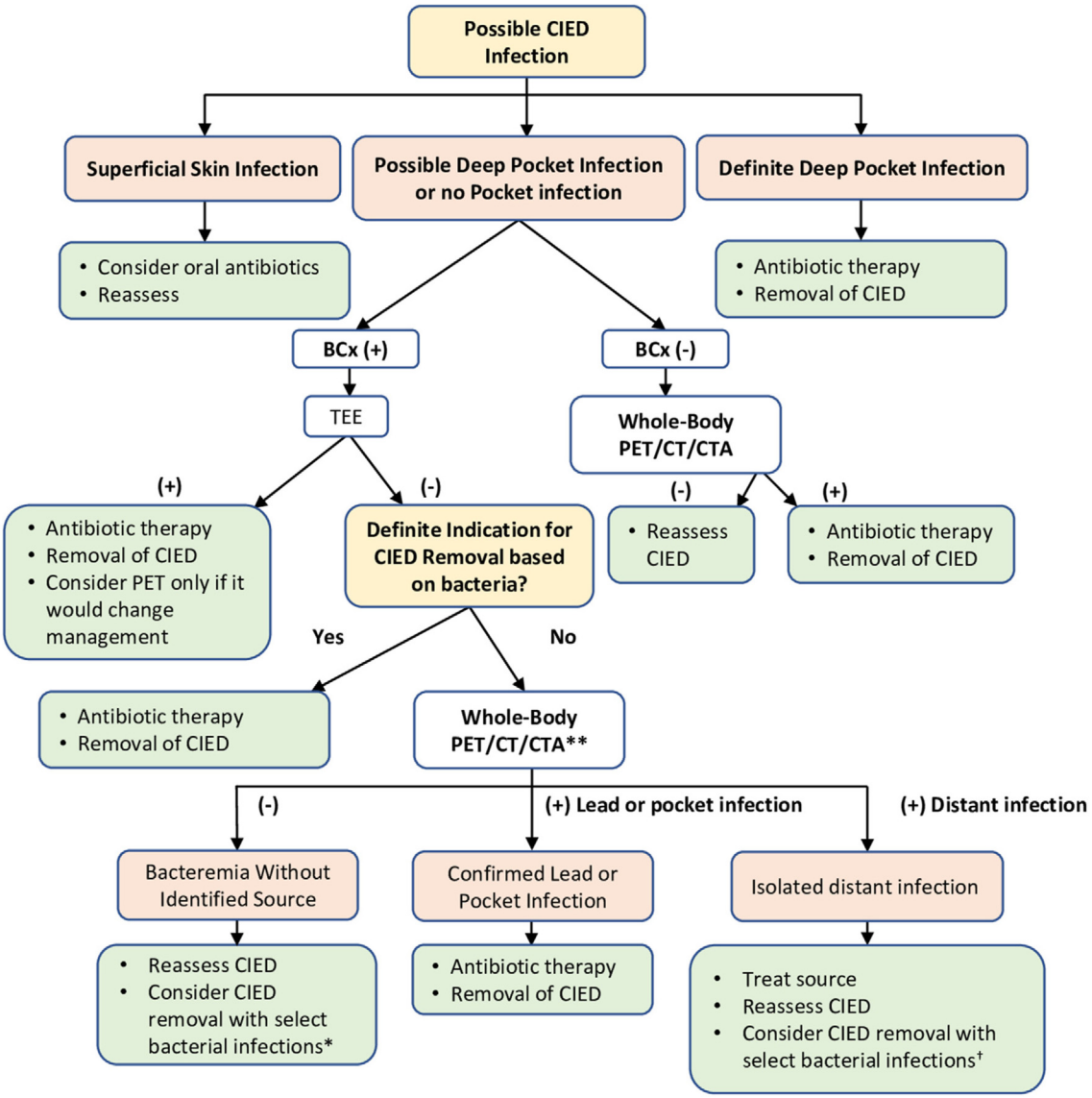

Figure 2

Diagnostic Algorithm Flowchart for Suspected CIED Infection. A consensus algorithmic approach is provided for patients with suspected CIED infection that incorporates assessment of the pocket, bacteremia, leads, and distant infection to establish a diagnosis and guide management. * This algorithm does not address every clinical presentation in which CIED infection should be considered. Additional scenarios are provided in Table 5. Moreover, complications such as septic pulmonary emboli and concomitant valve infection are not addressed and may require additional testing and therapy. ** The role of ^{18}F-FDG PET/CT is not clear in patients with select bacteremias (e.g., pneumococcal, non-pseudomonal/non-Serratia gram-negative rod) from an identified portal of entry with a low-risk of CIED infection. † CIED removal should be considered in the setting of *Staphylococcus aureus*, coagulase-negative *staphylococcus*, *Propionibacterium*, and *candida* species[25,35]. Abx = antibiotics; BCx = blood cultures; CIED = cardiovascular implantable electronic device; Cardiac CTA = cardiac-gated computed tomography angiography (with contrast); CT = computed tomography (with contrast); PET = positron emission tomography; TEE = transesophageal echocardiography.

such, ^{18}F-FDG PET/CT May Be Appropriate if clinicians require information about embolic events, port of entry, or anatomic information pertaining to a perivalvular abscess to aid surgical decision-making[128,129]. ^{18}F-FDG PET/CT is considered Rarely Appropriate for monitoring therapy in NVE.

Radiolabeled leukocyte SPECT/CT scintigraphy generally has a lower sensitivity but higher specificity for the detection of infected foci compared to ^{18}F-FDG PET/CT. This is reflected in the ratings in which indications that are considered Appropriate for evaluation by ^{18}F-FDG PET/CT would be considered May Be Appropriate for radiolabeled leukocyte SPECT/CT. In most cases, ^{18}F-FDG PET/CT would be preferred over radiolabeled leukocyte SPECT/CT based on greater availability, superior test characteristics (including less waiting time: 1 hour vs 24 hours), and more available data to support its use. Given the low sensitivity of radiolabeled leukocyte SPECT/CT for the diagnosis of gram-negative and fungal infections, it is considered Rarely Appropriate to use in these settings. Given the specificity of radiolabeled leukocyte SPECT/CT for infection, it is considered Appropriate for use in FUO in a patient with IE risk factors, high suspicion for IE, negative initial evaluation, and suspected infected extracardiac hardware[130]. Use of high-sensitivity SPECT/CT cameras may improve the diagnostic performance in NVE[131].

Table 4 Appropriate utilization rating of ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT imaging in suspected native and prosthetic valve infective endocarditis.

Clinical Scenarios	Native Valves		Prosthetic Valves	
	^{18}F-FDG PET/CT	Radiolabeled Leukocyte SPECT/CT	^{18}F-FDG PET/CT	Radiolabeled Leukocyte SPECT/CT
1. Definite IE—Stable Clinical Status				
1.1 Suspected left-sided embolic event	M (*)	M (5)	A (7.5)	M (5)
1.2 Suspected right-sided embolic event	M (*)	M (5)	M (5.5)	M (4.5)
1.3 Confirmation of perivalvular complications: Echo/Cardiac CTA definite for presence of perivalvular abscess	M (5)	M (6.5)	R (2.5)	R (2.5)
1.4 Detection of perivalvular complications: Echo/Cardiac CTA equivocal for presence of perivalvular abscess	A (7)	M (5)	A (8)	A (7)
1.5 Detection of perivalvular complications: Echo/Cardiac CTA negative for presence of perivalvular abscess	R (3)	R (3)	M (4.5)	M (5)
Clarification of cause of perivalvular leak			M (5)	M (5)
1.6 Detection of infectious source or focus: Persistent bacteremia	A (7.5)	A (7)	A (8)	A (7)
1.7 Detection of infectious source or focus: Presence of hardware	A (7.5)	A (7)	A (8)	A (7.5)
1.8 Monitoring of therapy	R (2.5)	R (3)	M (5)	M (5)
2. Possible IE or IE Rejected by Modified Duke-Li Criteria but High Clinical Suspicion				
2.1 Gram-positive bacteremia with negative echo—Typical organism for IE**	A (7.5)	M (5)	A (8)	A (7.5)
2.2 Gram-positive bacteremia with negative echo—Atypical organism for IE	A (7.5)	M (5)	A (7.5)	A (7.5)
2.3 Gram-negative bacteremia with negative echo—Typical organism for IE (HACEK)†	A (7.0)	M (*)	A (7.5)	M (5.5)
2.4 Gram-negative bacteremia with negative echo—Atypical organism for IE (non-HACEK)	M (5)	M (*)	A (7.5)	M (5)
2.5 Fungemia with negative echo	M (5)	R (2)	A (7.5)	R (1.5)
2.6 Inconclusive echo or discrepant imaging results	A (7.5)	M (*)	A (8)	A (7.5)
2.7 Persistent bacteremia or sepsis	M (6)	M (5)	A (7.5)	M (5.5)
2.8 Persistent fungemia	M (5.5)	R (2)	A (7.5)	R (1.5)
2.9 Blood cultures/serology negative but mobile mass on echocardiography	A (7.5)	M (5)	A (7.5)	M (5.5)
2.10 Elevated gradient across transcatheter prosthetic valve with suspicion of infection			A (7.0)	M (5.5)
2.11 Diffuse moderate FDG signal in the prosthesis in a patient with fever or inflammatory syndrome and negative echocardiography				M (*)
2.12 Absent FDG signal in the prosthesis in a patient with fever or inflammatory syndrome and negative echocardiography				R (2.5)
3. IE Rejected by Modified Duke-Li Criteria and Low Clinical Suspicion				
3.1 Fever of unknown origin—Risk factors for IE (IVDA, prior valve surgery, implanted cardiac devices, prosthetic material, congenital heart disease)†	A (7.5)	A (7)	M (*)	M (5)
3.2 Fever of unknown origin—No risk factors	M (5)	R (2)	M (5)	M (5)

* There was a lack of consensus on this rating; a "May Be Appropriate" rating was assigned by convention.

**Typical gram-positive organisms for IE: *Staphylococcus aureus*; coagulase-negative *Staphylococcus*; some strains of *Streptococci; Enterococci*. Typical gram-negative organisms for IE: HACEK organisms (*Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species).

† In cases of PVE with aortic root replacement, both tables 3 and 5 would apply

Ratings are given as appropriate (A with green highlighting), may be appropriate (M with yellow highlighting), or rarely appropriate (R with red highlighting) with the mean rating given in parentheses.

Cardiac CTA=cardiac-gated computed tomography angiography; Echo=echocardiogram; FDG=fluorodeoxyglucose; IE=infective endocarditis; IVDA=intravenous drug abuse; PET=positron emission tomography; SPECT=single photon emission computed tomography.

Table 5 Appropriate utilization rating of ^{18}F-FDG PET/CT in suspected CIED Infection.*

Clinical Scenarios	^{18}F-FDG PET/CT
No Evidence of Systemic Infection in suspected CIED infection	
High clinical suspicion of superficial infection only	R (2.5)
Unclear determination superficial vs. CIED pocket infection	A (7)
High clinical suspicion for CIED pocket infection	M (5)
Fever of unknown origin with negative TEE	A (7)
Mobile mass on TTE/TEE but no other evidence of systemic infection	M (4.5)
Evidence of Systemic Infection: No Imaging Evidence of Vegetations on CIED	
Gram-positive bacteremia with typical organism†	M (5.5)
Gram-positive bacteremia with atypical organism	M (5.5)
Gram-negative bacteremia with typical organism†	M (6)
Gram-negative bacteremia with atypical organism	M (5.5)
Fungemia	M (5.5)
Evidence of Systemic Infection: Imaging Evidence of Vegetations on CIED	
Gram-positive bacteremia with typical organism†	R (2.5)
Gram-positive bacteremia with atypical organism	R (2.5)
Gram-negative bacteremia with typical organism†	R (2.5)
Gram-negative bacteremia with atypical organism	R (2.5)
Fungemia	R (2.5)
Evidence of Systemic Infection: Imaging Equivocal or Non-Diagnostic for Vegetations on CIED	
Gram-positive bacteremia with typical organism†	A (8)
Gram-positive bacteremia with atypical organism	A (7.5)
Gram-negative bacteremia with typical organism†	A (7.5)
Gram-negative bacteremia with atypical organism	A (7)
Fungemia	A (7.5)

* Ratings are not provided for radiolabeled leukocyte SPECT/CT due to inadequate data.

† Typical gram-positive organisms for IE: *Staphylococcus aureus*, coagulase negative *Staphylococcus*, *Cutibacterium* species). Typical gram-negative organisms for IE: HACEK organisms (*Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species); *Serratia* species and *Pseudomonas aeruginosa* (Data are limited with respected to gram-negative rods and CIED-related IE).

Ratings are given as appropriate (A with green highlighting), may be appropriate (M with yellow highlighting), or rarely appropriate (R with red highlighting) with the mean rating given in parentheses.

CIED=cardiovascular implantable electronic device; CT=computed tomography; FDG=fluorodeoxyglucose; PET=positron emission tomography; TEE=transesophageal echocardiography; TTE=transthoracic echocardiography.

Prosthetic valve endocarditis

There are many indications for ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT in the diagnosis of PVE. These imaging modalities can help confirm suspected infection and guide the management of these cases, including aiding surgical intervention decision-making[132]. ^{18}F-FDG PET-CT ideally is performed as soon as possible, as increasing duration of antibiotic therapy reduces test sensitivity[133]. Although not addressed as a distinct clinical indication in this document, transcatheter-implanted aortic valve IE will likely increase in incidence with growing utilization and remains difficult to diagnose due to mild, nonspecific clinical presentation and limited role of echocardiography[92]. ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT may prove to be a valuable diagnostic tool in this population[134].

When echocardiography is negative or equivocal for PVE, but clinical suspicion is high, ^{18}F-FDG PET/CT or radiolabeled leukocyte SPECT/CT (when ^{18}F-FDG PET/CT is unavailable or inconclusive) is Appropriate. Both imaging modalities are strongly recommended in cases with gram-positive infections[24]. Fungal infections have been noted to cause false-negative radiolabeled leukocyte SPECT/CT studies due to the relative low accumulation of neutrophils compared to other infections[135]. ^{18}F-FDG PET/CT is the preferred imaging study for diagnosing PVE in cases of fungal infections[85–87,136]. Radiolabeled leukocyte SPECT/CT also has a lower sensitivity for the diagnosis of certain gram-negative infections thus, ^{18}F-FDG PET/CT is preferred for these cases as well. However, if ^{18}F-FDG PET/CT imaging is not available and echocardiography is equivocal in cases with gram-negative organisms, radiolabeled leukocyte SPECT/CT may still be considered.

In patients with and without risk factors for PVE who have a negative standard workup but present with FUO, ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT May Be Appropriate in select cases[94]. However, there was not consensus among the rating panel whether ^{18}F-FDG PET/CT is helpful in such cases. When PVE has already been

Table 6 Appropriate utilization rating of ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT imaging in suspected prosthetic material infection.

Clinical Scenarios	^{18}F-FDG PET/CT	Radiolabeled Leukocyte SPECT/CT Imaging
No Evidence of Systemic Infection		
Fever of unknown origin	M (5)	M (5)
Elevated inflammatory markers	R (2.5)	R (2.5)
Evidence of Systemic Infection: No Imaging Evidence of Prosthetic Material Infection		
Gram-positive bacteremia with typical organism*	A (7.5)	M (5)
Gram-positive bacteremia with atypical organism	A (7.5)	M (5)
Gram-negative bacteremia with typical organism*	A (7.5)	M (5)
Gram-negative bacteremia with atypical organism	M (5.5)	M (5)
Fungemia	M (*)	R (2)
Evidence of Systemic Infection: Imaging Evidence of Prosthetic Material Infection		
Gram-positive bacteremia with typical organism*	M (5.5)	R (2.5)
Gram-positive bacteremia with atypical organism	M (5)	R (2.5)
Gram-negative bacteremia with typical organism*	M (5.5)	R (2.5)
Gram-negative bacteremia with atypical organism	M (5)	R (2)
Fungemia	M (5.5)	R (2)
Evidence of Systemic Infection: Imaging Equivocal or Non-Diagnostic for Prosthetic Material Infection		
Gram-positive bacteremia with typical organism*	A (8)	A (8)
Gram-positive bacteremia with atypical organism	A (7.5)	A (7.5)
Gram-negative bacteremia with typical organism*	A (8.0)	A (8)
Gram-negative bacteremia with atypical organism	A (7.5)	M (*)
Fungemia	A (7.5)	R (2)
Additional considerations for any of the appropriate indications above		
Patient in whom bioadhesive was used during surgery	M (5)	A (7)
Patient with congenital heart disease	A (7)	A (7.5)

* Typical gram-positive organisms for prosthetic material infection: *Staphylococcus aureus*, coagulase negative *Staphylococcus*, *Enterococci* species, *Corynebacterium* species, *Cutibacterium* species. Typical gram-negative organisms for prosthetic material infection: *Pseudomonas aeruginosa*, *Escheria* coli, Klebsiella species, *Salmonella* species, and anaerobes in the setting of abdominal grafts. Fungemia with *Candida* species is also possible in the setting of broad-spectrum antibiotic use or in abdominal grafts.

Ratings are given as appropriate (A with green highlighting), may be appropriate (M with yellow highlighting), or rarely appropriate (R with red highlighting) with the mean rating given in parentheses. CT=computed tomography; FDG=fluorodeoxyglucose; PET=positron emission tomography; SPECT=single-photon emission computed tomography.

diagnosed by echocardiography, ^{18}F-FDG PET/CT or radiolabeled leukocyte SPECT/CT (when ^{18}F-FDG PET/CT is unavailable or inconclusive) is Appropriate to assess for perivalvular complications, such as abscess when echocardiography is equivocal, and May Be Appropriate to exclude active infection next to a paravalvular leak prior to intervention. Cardiac CTA can identify perivalvular complications, but FDG uptake can be additive by confirming the presence of active inflammation. In the setting of persistent bacteremia in patients with PVE and/or the presence of other prosthetic material, ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT are recommended, as they can be useful detecting extracardiac foci of infection or identifying other portals of entry. Preliminary data suggest ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT may be useful in monitoring cases of PVE that are medically managed with antimicrobial treatment, but further studies are needed to inform the frequency and reliability of monitoring strategies. The role of these advanced modalities in assessment of suspected embolic events in both NVE and PVE is not fully elucidated but is recommended by the ESC guidelines workflow[24].

CIED infection

CIED infections encompass both local (device pocket), systemic (bloodstream and/or lead-related), or combined infections. Pocket infections can be superficial incisional cellulitis or deep infection involving the underlying pocket, which requires more aggressive therapy. Deep pocket infections, often involving the pulse generator and leads, are more serious and necessitate device extraction for source control. The role of advanced nuclear imaging in device infection is most valuable when the depth of infection and hardware involvement is unclear. For example, in patients with strictly superficial infections that resolve with oral antibiotics, or bacteremic patients with clear imaging evidence of vegetations on the CIED, ^{18}F-FDG PET/CT imaging is Rarely

Table 7 Appropriate utilization rating of ^{18}F-FDG PET/CT in suspected ventricular assist device infection.

Clinical Scenarios	^{18}F-FDG PET/CT
No Evidence of Systemic Infection	
Concern for central hardware VAD infection (cannula or pump)	A (7.5)
Concern for peripheral exit wound infection	R (2.5)
Concern for driveline infection	A (7)
Concern for sternal wound infection	M (4.5)
Evidence of Systemic Infection	
Bacteremia without identifiable source*	A (8)
Fungemia without identifiable source	A (7.5)
Persistent Bacteremia	A (8)
Persistent Fungemia	A (8)
Fever of unknown origin	A (7.5)
Unexplained embolic phenomena	A (7.5)
Device dysfunction/thrombosis	M (5.5)
Additional considerations for any of the appropriate indications above	
Patient in whom bioadhesive was used during surgery	M (4.5)

*Typical gram-positive organisms for VAD infection: *Staphylococcus aureus*, coagulase negative *Staphylococcus*, *Enterococci* species. Typical gram-negative organisms for VAD infection: *Pseudomonas aeruginosa*, *Serratia* species, and *Enterobacteriaceae*.

Ratings are given as appropriate (A with green highlighting), may be appropriate (M with yellow highlighting), or rarely appropriate (R with red highlighting) with the mean rating given in parentheses. VAD=ventricular assist device.

Appropriate. However, patients in whom the distinction of deep versus superficial pocket infection is unclear, ^{18}F-FDG PET/CT imaging has high diagnostic accuracy to identify pocket/generator infection[137] and is considered Appropriate. ^{18}F-FDG PET/CT imaging is also Appropriate to confirm lead infection in bacteremic patients with equivocal vegetations. Because ^{18}F-FDG PET/CT imaging has a high positive predictive value but lower negative predictive value, it cannot definitively rule out CIED infection and is thus rated May Be Appropriate in patients with evidence of systemic infection and no vegetations on imaging.

^{18}F-FDG PET/CT imaging diagnostic performance is lower for lead than for pocket infection[137]. Detection of lead infection can be improved by shortening the delay between antibiotic initiation and imaging and by adding late PET acquisitions (90-180 min post-injection) in patients with persistent high blood pool ^{18}F-FDG signal using typical protocols[71,89]. The presence of focal ^{18}F-FDG uptake in the lung parenchyma should raise the suspicion of septic emboli, which are often associated with lead infection[89]. Importantly, lead infection cannot be excluded if the ^{18}F-FDG PET/CT scan is negative. In the absence of systemic infection but increased clinical suspicion, options for diagnosis of CIED infection are limited, and ^{18}F-FDG PET/CT imaging was rated as May Be Appropriate. For patients presenting with a new lead mass on echocardiography but no evidence of systemic infection, ^{18}F-FDG PET/CT imaging May Be Appropriate to discriminate between thrombus and vegetation. This indication should be approached with caution, however, as non-infective mobile echo densities are frequent on CIED leads, and additional imaging should only be considered in select cases with higher clinical suspicion. In patients with CIED and FUO with negative TEE, ^{18}F-FDG PET/CT imaging is Appropriate to confirm CIED infection and might be also helpful to detect the alternative causes of FUO. Diagnostic yield may be lower in the setting of bacteremia or symptoms of short duration and repeatedly normal TEE.

It is important to note that patients with clear evidence of infection irrespective of imaging, such as those with prolonged bacteremia, especially with typical organisms, have an indication for CIED removal, and this definitive therapy should not be delayed to obtain ^{18}F-FDG PET/CT imaging.

Although rating was performed for ^{18}F-FDG PET/CT as detailed above, the panel did not rate radiolabeled leukocyte SPECT/CT in CIED infection due to insufficient evidence to support appropriate use criteria for this imaging modality at this time. Radiolabeled leukocyte SPECT/CT imaging has higher specificity but lower sensitivity than ^{18}F-FDG PET/CT imaging for infection[89]. There is emerging evidence of a possible role to distinguish infective from inflammatory processes in the CIED pocket, particularly in patients with positive ^{18}F-FDG PET/CT scans within the first weeks of device implantation.

Prosthetic material infection

Infections of cardiac prosthetic material typically are diagnosed using echocardiography and contrast enhanced CT. However, certain clinical scenarios may require advanced imaging with ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT. When clinical suspicion for an infection is high with fever but no source of infection is identified despite extensive investigation (FUO), ^{18}F-FDG PET/CT May Be Appropriate[94]. In contrast, when a patient has elevated

inflammatory markers but no fever or other evidence of systemic infection, ^{18}F-FDG PET/CT is Rarely Appropriate.

In the setting of systemic infection with persistent (not transient) bacteremia and negative imaging findings for prosthetic material infection on other modalities (such as echo, CT), ^{18}F-FDG PET/CT is Appropriate to localize the source of bacteriemia and to evaluate for seeding sites in gram-positive or typical gram-negative organisms. A negative ^{18}F-FDG PET/CT in this setting will effectively rule out prosthetic material infection. Infection with less suspicious organisms (gram-negative atypical) or with fungemia received a May Be Appropriate rating, as did use of radiolabeled leukocyte SPECT/CT due to its reduced sensitivity (excluding fungemia).

If there is systemic infection and evidence of infected prosthetic material on other imaging modalities, ^{18}F-FDG PET/CT is not necessary for diagnosis. Nonetheless, ^{18}F-FDG PET/CT may have a role in providing prognostic information as well as identifying portal of entry and embolic events, but only if an active search for portal of entry or embolic event will change clinical management. In complex cases where removal of the prosthetic material is challenging or has increased consequences, ^{18}F-FDG PET/CT may be helpful in surgical planning or monitoring treatment response in cases where medical therapy is used alone. Radiolabeled leukocyte SPECT/CT is less useful for this purpose, as it has poor resolution and will be of limited use in guiding surgery. In patients in whom imaging was equivocal for a prosthetic material infection, both ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT were rated as Appropriate.

One clinical scenario where radiolabeled leukocyte SPECT/CT has an advantage over ^{18}F-FDG PET/CT is the evaluation for infected prosthetic material for patients in whom bioadhesive was used during their surgeries because certain bio adhesives cause persistently elevated ^{18}F-FDG uptake and results in false-positive ^{18}F-FDG scan or masks an underlying true infection[138]. A heterogenous pattern of uptake may help to differentiate true from false-positive uptake, but these cases are challenging and must be approached with caution. Thus, ^{18}F-FDG PET/CT May Be Appropriate in this scenario. However, radiolabeled leukocyte SPECT/CT was rated as Appropriate as an alternative in these patients, as leukocytes do not typically artifactually accumulate at the site of bioadhesive.

In patients with congenital heart disease, ^{18}F-FDG PET/CT can help with diagnosis when echocardiography is negative, in the setting of suspected PVE, and—in particular—for patients with right-sided grafts[46,139]. Special consideration is also given in patients with congenital heart disease who have prosthetic material that cannot be removed or is very difficult to remove, such as with right ventricle–pulmonary artery conduits and Blalock-Taussig shunts. When such prosthetic material is infected, the mainstay of treatment is long-term antibiotics. In some centers, ^{18}F-FDG PET/CT is used for monitoring response and determination of recommended treatment duration[46,139]. Radiolabeled leukocyte SPECT/CT is also Appropriate in such scenarios but is less favored due to its inherent lower sensitivity.

VAD infection

The International Society of Heart and Lung Transplantation has separated suspected VAD infection into three categories: (1) VAD-specific infection (central hardware, including pump, cannula, and peripheral percutaneous driveline); (2) VAD-related infection (blood stream infection, sternal wound infection, and mediastinitis); and (3) non-VAD infection (not directly related to the VAD), such as pneumonia and urinary tract infection in patients carrying VAD hardware[116]. Radiolabeled leukocyte SPECT/CT has insufficient data in suspected VAD infection and was not rated by the panel. ^{18}F-FDG PET/CT has variable roles for the three types of VAD infection. For VAD-specific infection, ^{18}F-FDG PET/CT is Appropriate for evaluation of suspected central hardware and peripheral subcutaneous driveline infection. Identification of infection site as central hardware or peripheral driveline may affect patient's management and outcome[140]. Although driveline exit-site infection is the most common type of infection due to local trauma during daily activity and is a frequent source of central infection, ^{18}F-FDG PET/CT is Rarely Appropriate for evaluation of suspected infection limited to the exit site alone, as this can be assessed and diagnosed on physical examination. It May Be Appropriate in evaluating possible sternal wound infection.

^{18}F-FDG PET/CT was rated as Appropriate for evaluation of VAD-related infection in patients with evidence of systemic infection who have bacteremia or fungemia without an identifiable source or that is persistent, FUO, or unexplained embolic phenomena. In the setting of systemic infection, device dysfunction/thrombosis may indicate VAD involvement. In this context, ^{18}F-FDG PET/CT was rated as May Be Appropriate for the evaluation of these patients.

Clinical cases

Case #1. Prosthetic valve endocarditis assessed with ^{18}F-FDG PET/CT

A 65-year-old woman with history of a bioprosthetic bovine aortic valve replacement and ascending aortic graft placement for thoracic aortic aneurysm eight years prior presented with a fever of 38.9 °C. Multiple blood cultures grew *Lactobacillus rhamnosus,* a gram-positive anaerobe that is an atypical organism for IE. She had bacteremia with the same organism 3 months prior to the fever with a negative TEE evaluation and received 6 weeks of antibiotic therapy. Due to a penicillin allergy, she was treated with IV daptomycin for 1 week followed by 5 weeks of IV clindamycin. Surveillance blood cultures after completion of her antibiotic course were negative. Her evaluation included an abdomen and pelvis CT scan and a transthoracic echocardiogram during the same admission that was both unremarkable. TEE showed no evidence of aortic valvular or paravalvular regurgitation or bioprosthetic stenosis. There was no evidence of an independently mobile echo density or paravalvular abscess. ^{18}F-FDG PET/CT was performed on day 8 of her hospitalization following a 24-hours ketogenic diet and overnight fast (Figure 3). Eight mCi (296 MBq) of ^{18}F-FDG was administered

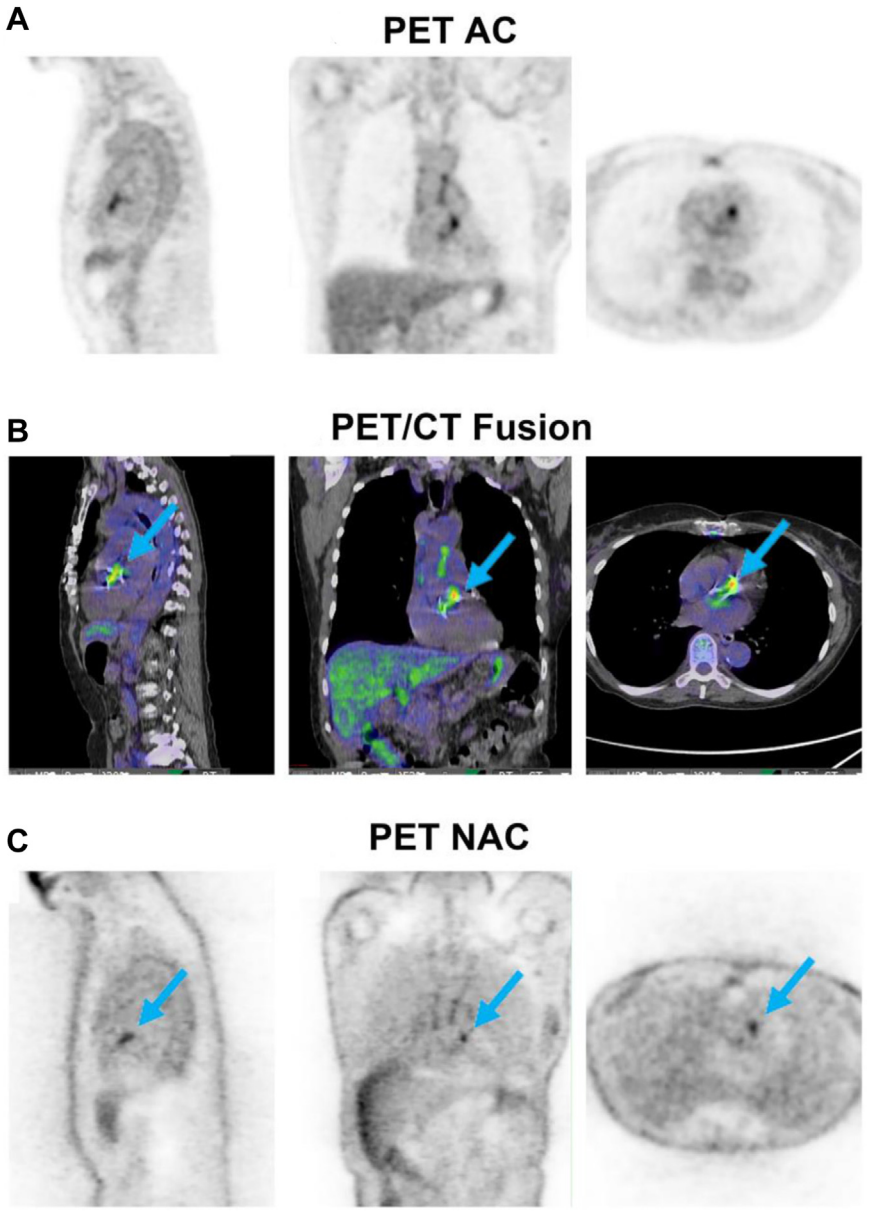

Figure 3
Prosthetic Valve Endocarditis Assessed with ^{18}F-FDG PET/CT. Sagittal, coronal, and axial images show focal, intense uptake along the anterior/left lateral aspect of the prosthetic aortic valve on attenuation corrected (panel A) and CT-fused images (arrows, panel B) that persists on the non-attenuation corrected images (arrows, panel C), confirming PVE. Mild diffuse aortic wall uptake was considered physiological. Whole-body imaging revealed no evidence of septic emboli.

intravenously followed by cardiac and whole-body PET/CT imaging after a 60-minutes delay. The ^{18}F-FDG PET/CT images identified a focal, perivalvular infectious process. Based on these results, definite PVE was diagnosed. Surgical intervention was not deemed necessary given her lack of active infectious symptoms, lack of valvular dysfunction, and negative blood cultures. She was medically managed with prolonged antibiotics (6-weeks IV followed by one-year oral) without further complications on more than three years follow-up.

This case illustrates the role of ^{18}F-FDG PET/CT and its appropriate use in the evaluation of suspected IE in prosthetic valves. This patient had one major and two minor 2015 Duke/ESC criteria and was classified as possible IE. Given her recent history of infection, the team had high clinical suspicion for PVE, and ^{18}F-FDG PET/CT confirmed PVE (see diagnostic algorithm in Figure 1). The use of ^{18}F-FDG PET/CT to assess possible IE in the setting of gram-positive bacteremia with a negative echocardiogram and an atypical organism for IE is considered Appropriate as rated in Table 4.

Case #2. Prosthetic valve endocarditis assessed with radiolabeled leukocyte SPECT/CT

A 74-year-old woman with diabetes mellitus and polymyalgia rheumatica underwent prior mitral and aortic valve replacements more than 25 years prior. She had previous atrial fibrillation complicated by cerebral ischemia and left-leg arterial occlusive disease. She presented to the Emergency

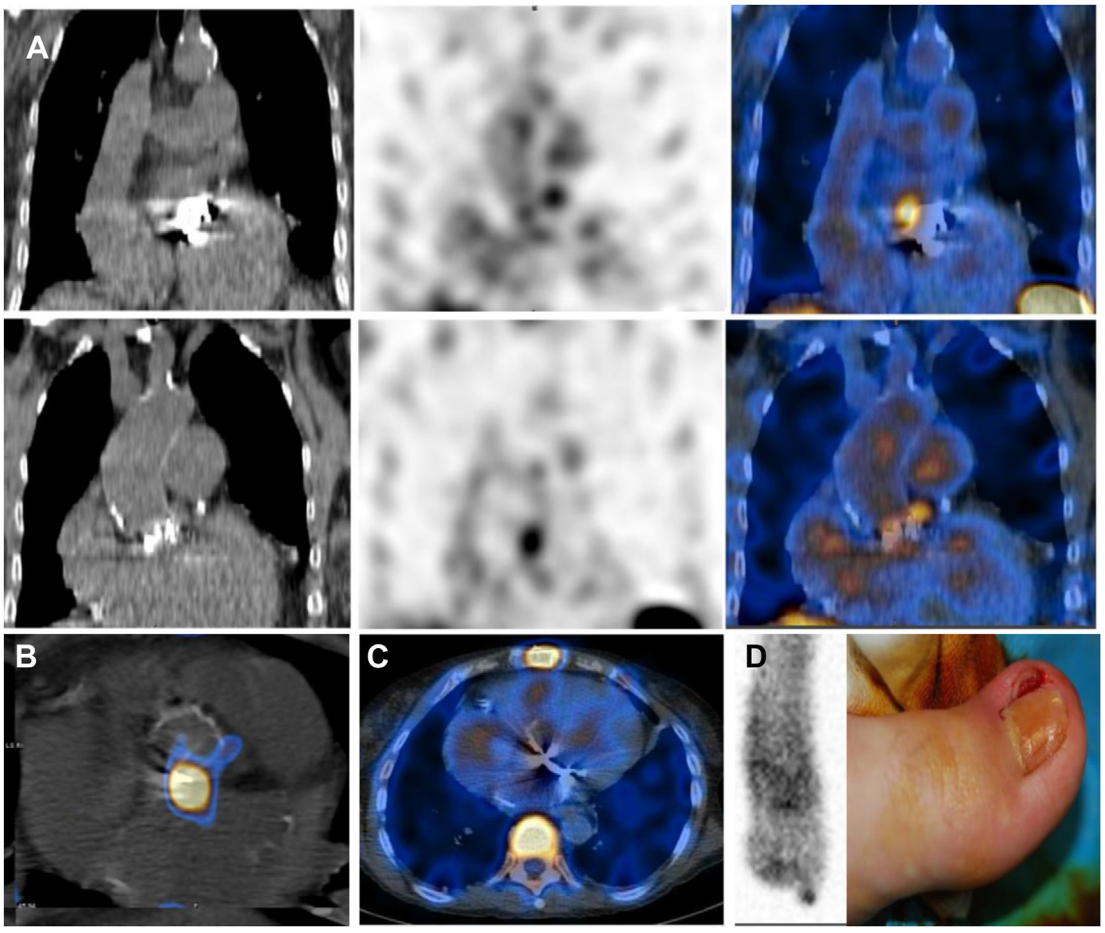

Figure 4
Prosthetic Valve Endocarditis Assessed with Radiolabeled Leukocyte SPECT/CT. CT, attenuation-corrected SPECT, and fused images reveal abnormal intense, focal uptake in panel A. The abnormal focus is localized to the posterior aspect of the prosthetic aortic valve (panel B) with no involvement of the mitral valve appreciated (panel C). A distal infected focus in the left great toe was appreciated on whole-body imaging (panel D). These image findings were consistent with PVE with distal embolic involvement.

Department with recurrent fever, which was treated with empiric antimicrobial therapy. The patient underwent a TTE, TEE, chest CT scan, and abdominal ultrasound, all of which were unrevealing. Laboratory testing showed increased erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), a positive urine culture (*Proteus Mirabilis*) and two sets of blood cultures that grew *Enterococcus faecalis*, a gram-positive bacterium typical for IE.

She was classified as possible IE per the Duke/ESC 2015 criteria, and there was high clinical suspicion. There were three possible clinical strategies considered: (1) treat the patient empirically; (2) repeat TTE/TEE in 5–7 days; or (3) perform an advanced radionuclide imaging procedure. Due to the presence of a possible concomitant bone infection of the left great toe (hallux), a whole-body ^{99m}Tc-HMPAO radiolabeled leukocyte scan, including SPECT/CT of the chest was obtained 6 hours after injection. Abnormal aortic valve prosthetic uptake and left great-toe abnormality was present consistent with PVE with distal embolic involvement (Figure 4, panels A–D). The toe infection was diagnosed as osteomyelitis, and she was managed successfully with amputation. The patient received 8 weeks of intravenous followed by oral antibiotics, and cardiac surgery was deferred due to high surgical risk. Nevertheless, she remained complication-free at 6 months follow-up.

This case illustrates the role of radiolabeled leukocyte SPECT/CT and its appropriate use in the evaluation of suspected IE in prosthetic valves. The advanced imaging procedure was favored per the diagnostic algorithm in this document (Figure 1) given her possible IE and high clinical suspicion. She had a May Be Appropriate indication for radiolabeled leukocyte SPECT/CT with possible IE and gram-positive bacteremia with a typical organism for IE (Table 4).

Case #3. Suspected lead CIED infection assessed with ^{18}F-FDG PET/CT

A 45-year-old woman was referred for evaluation of suspected CIED infection. She had a history of hypertrophic cardiomyopathy with primary prevention ICD placement and developed skin redness over the device pocket. She underwent blood cultures, which were negative. She underwent a whole-body ^{18}F-FDG PET/CT exam (Figure 5, Panels A and B) after a 12-

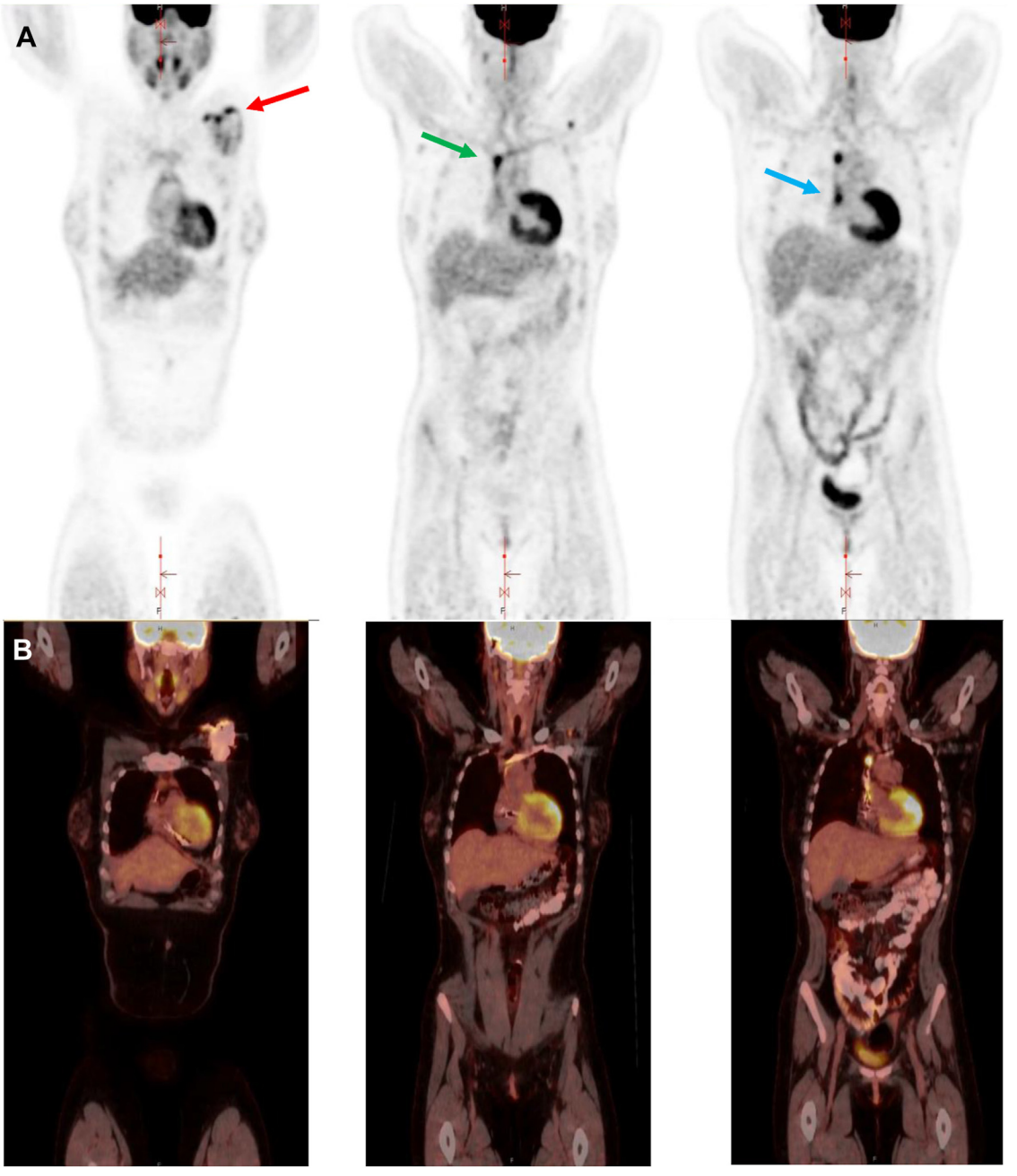

Figure 5
CIED Pocket and Lead Infection Diagnosed by ^{18}F-FDG PET/CT. Coronal PET images (panel A) show multiple areas of focal, heterogenous, intense ^{18}F-FDG uptake surrounding the ICD generator (standardized uptake value, SUVmax 4.8, red arrow), along the ICD leads (SUVmax 6, green arrow) and associated with the ICD leads in the right atrium (SUVmax 5.9, blue arrow). Uptake persisted on non-attenuation corrected images (not shown). Fusion with CT (panel B) confirm the anatomic localization. These findings confirmed CIED deep pocket infection with lead involvement.

hours fast (ketogenic diet was not feasible due to time considerations, and thus myocardial suppression was not achieved). The abnormal device and lead uptake suggested CIED infection with associated lead involvement. The generator and leads were subsequently removed; cultures of the removed hardware grew coagulase negative *Staphylococcus*. The patient was treated with antibiotics, and a new device was reimplanted after a 1-month delay.

This case illustrates the role of ^{18}F-FDG PET/CT and its appropriate use in the evaluation of suspected CIED infection. In the setting of a possible deep-pocket infection and negative blood cultures, whole-body ^{18}F-FDG PET/CT is recommended per the diagnostic algorithm in Figure 2. ^{18}F-FDG PET/CT is rated as Appropriate for unclear determination of superficial versus CIED pocket infection in the absence of evidence of systemic infection (Table 5). While this case demonstrates the utility of a positive FDG scan in the assessment of CIED infection, a negative scan would not necessarily have eliminated the possibility of CIED involvement, and further clinical and laboratory investigations would have been appropriate.

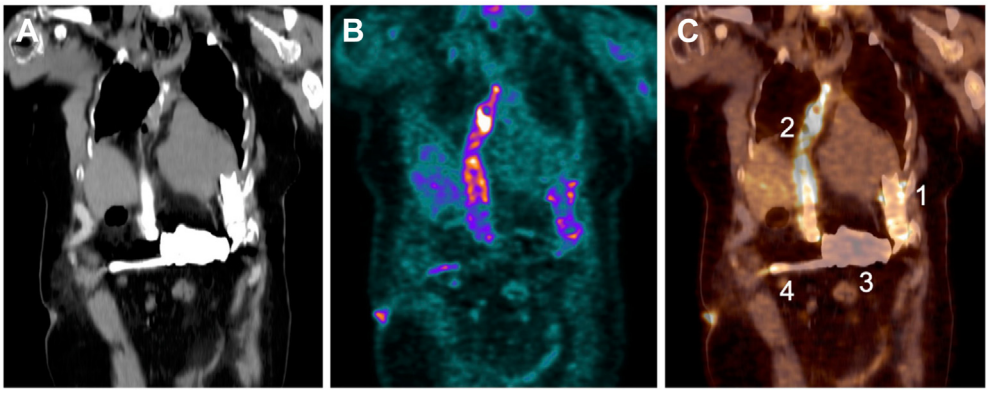

Figure 6

Extent of VAD Infection Clarified by ^{18}F-FDG PET/CT. Coronal CT images (panel A) are unrevealing for extent of infection. ^{18}F-FDG PET imaging (panel B) and fused PET/CT images (panel C) reveal heterogeneous, multifocal, intense uptake around the inflow (1) and outflow (2) cannulas and multiple portions of the driveline (4). There is no uptake in the pump area (3). These findings are consistent with central device and peripheral driveline infections.

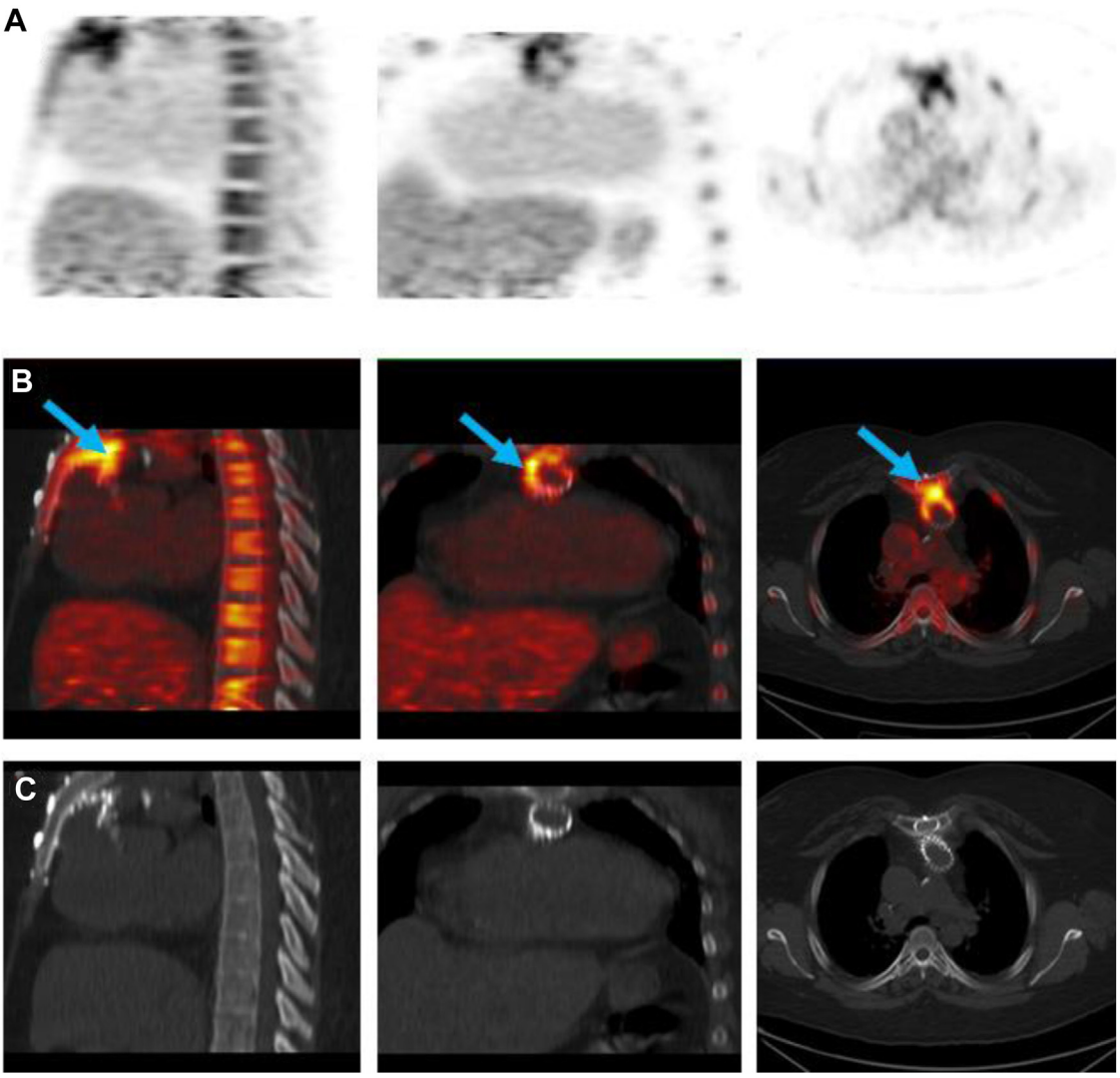

Figure 7

Prosthetic Material Infection Identified by ^{18}F-FDG PET/CT. Sagittal (left column), coronal (middle column) and axial slices (right column) are shown. The top row (panel A) shows ^{18}F-FDG images, the middle row (panel B) shows fused ^{18}F-FDG and CT images, and the bottom row (panel C) shows non-contrast attenuation correction CT images. There is focal, intense, heterogeneous ^{18}F-FDG uptake along the outflow conduit graft, with more focal uptake extending along the lateral aspect proximally and the anteromedial aspect distally (blue arrows). These findings are consistent with prosthetic graft infection.

Case #4. Suspected VAD infection assessed with ^{18}F-FDG PET/CT

A 43-year-old man with a history of idiopathic non-ischemic cardiomyopathy and congestive heart failure had undergone HeartMate II LVAD implantation two years previously as a bridge-to-heart transplantation. Since then, he has had multiple infections of the LVAD peripheral driveline for which he was treated with antibiotics. He was subsequently hospitalized for foul smelling pus draining out of the driveline site. Wound and blood cultures were positive for *Proteus mirabilis* compatible with a peripheral driveline infection with evidence of systemic infection. ^{18}F-FDG PET/CT was performed to evaluate for infection and revealed central device infection with confirmation of peripheral driveline involvement (Figure 6). Broad-spectrum antibiotics were started, and the patient was referred for surgical evaluation.

This case illustrates the use of ^{18}F-FDG PET/CT in suspected LVAD infection. As per Table 7, ^{18}F-FDG PET/CT is rated Appropriate to further evaluate extent of infection in the LVAD (central portion of the cannula and pump) in a patient with bacteremia without identifiable source but evidence of systemic infection.

Case #5. Suspected prosthetic material infection assessed with ^{18}F-FDG PET/CT

A 29-year-old female with a history of tetralogy of Fallot, status-post repair with a 22-mm right ventricle to pulmonary artery conduit and status-post transcatheter SAPIEN pulmonary valve placement four years prior presented with suspected PVE in setting of viridans streptococci bacteremia. ^{18}F-FDG PET/CT was obtained to determine whether the conduit or the valve was infected (Figure 7, Panels A and B). The patient received a preparatory high-fat/low-carbohydrate diet 24 hours prior to the study followed by an overnight fast. Abnormal graft uptake with this patient's history was thought to represent areas of infection. She was managed with aggressive antibiotic therapy, but one year later developed progressive pulmonary stenosis and regurgitation as well as tricuspid regurgitation on echocardiography. She underwent repeat cardiac surgery with excision of the SAPIEN pulmonary valve, pulmonary valve replacement with a 27 mm Magna Ease valve, and right ventricular outflow tract reconstruction with bovine pericardium and tricuspid valve repair. Culture of the excised valve confirmed the infection.

This case illustrates the role of ^{18}F-FDG PET/CT and its appropriate use in the evaluation of prosthetic material infection. Imaging was Appropriate to assess gram-positive bacteremia with a typical organism and no imaging evidence of prosthetic material involvement (Table 6).

Conclusions

This document has summarized expert recommendations on the appropriate use of ^{18}F-FDG PET/CT and radiolabeled leukocyte SPECT/CT in the evaluation and management of cardiovascular infection. Moreover, key points on multimodality imaging in cardiovascular infection and multisocietal expert consensus on diagnostic features on radionuclide imaging were provided with an algorithmic approach to use for this advanced imaging and the appropriateness of relevant clinical indications, with case studies highlighting its practical applications. These ratings highlight that evidence demonstrates usefulness but do not imply need to perform advanced imaging. Study performance should be carefully considered in each individual case by the experts of the local Endocarditis Team in order to match test performance with appropriate clinical suspicion. Moreover, this process has identified gaps in the literature requiring future research. Further investigation is warranted to validate the recommendations of this consensus document and to provide the basis for revised guidelines on cardiovascular infection within the next few years. We intend for this consensus statement to be used as a model for inclusion of nuclear imaging into a multimodality approach with feedback incorporated from relevant clinical and imaging societies.

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Correspondence: MHS Associate Professor of Medicine and Radiology Cardiovascular Division, Departments of Medicine and Radiology University of Virginia Health System, Box 800158 1215 Lee Street, Charlottesville, VA 22908, USA. E-mail address: JMB8T@uvahealth.org. (Jamieson M. Bourque).

References

1. Bin Abdulhak AA, Baddour LM, Erwin PJ, Hoen B, Chu VH, Mensah GA, et al. Global and regional burden of infective endocarditis, 1990-2010: a systematic review of the literature. *Glob Heart* 2014;9(1):131–143. https://doi.org/10.1016/j.gheart.2014.01.002.
2. Pant S, Patel NJ, Deshmukh A, Golwala H, Patel N, Badheka A, et al. Trends in infective endocarditis incidence, microbiology, and valve replacement in the United States from 2000 to 2011. J Am Coll Cardiol 2015;65(19):2070–2076. https://doi.org/10.1016/j.jacc.2015.03.518.
3. Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB, Thornhill MH. Incidence of infective endocarditis in England, 2000-13: a secular trend, interrupted time-series analysis. *Lancet* 2015;385(9974):1219–1228. https://doi.org/10.1016/S0140-6736(14)62007-9.
4. Krahn AD, Longtin Y, Philippon F, Birnie DH, Manlucu J, Angaran P, et al. Prevention of Arrhythmia Device Infection Trial: The PADIT Trial. J Am Coll Cardiol 2018;72(24):3098–3109. https://doi.org/10.1016/j.jacc.2018.09.068.
5. Greenspon AJ, Patel JD, Lau E, Ochoa JA, Frisch DR, Ho RT, et al. 16-year trends in the infection burden for pacemakers and implantable cardioverter-defibrillators in the United States 1993 to 2008. J Am Coll Cardiol 2011;58(10):1001–1006. https://doi.org/10.1016/j.jacc.2011.04.033.
6. Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler VG Jr, Bayer AS, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med 2009;169(5):463–473. https://doi.org/10.1001/archinternmed.2008.603.
7. Selton-Suty C, Célard M, Le Moing V, Doco-Lecompte T, Chirouze C, Iung B, et al. Preeminence of Staphylococcus aureus in infective endocarditis: a 1-year population-based survey. *Clin Infect Dis* 2012;54(9):1230–1239. https://doi.org/10.1093/cid/cis199.
8. Tleyjeh IM, Abdel-Latif A, Rahbi H, Rahbi H, Scott CG, Bailey KR, et al. A systematic review of population-based studies of infective endocarditis. *Chest* 2007;132(3):1025–1035. https://doi.org/10.1378/chest.06-2048.
9. Morita Y, Haruna T, Haruna Y, Nakane E, Yamaji Y, Hayashi H, et al. Thirty-Day Readmission After Infective Endocarditis: Analysis From a Nationwide Readmission Database. J Am Heart Assoc 2019;8(9):e011598 https://doi.org/10.1161/JAHA.118.011598.
10. Tarakji KG, Mittal S, Kennergren C, Corey R, Poole JE, Schloss E, et al. Antibacterial Envelope to Prevent Cardiac Implantable Device Infection. *N Engl J Med* 2019;380(20):1895–1905. https://doi.org/10.1056/NEJMoa1901111.
11. Prutkin JM, Reynolds MR, Bao H, Curtis JP, Al-Khatib SM, Aggarwal S, et al. Rates of and factors associated with infection in 200 909 Medicare implantable cardioverter-defibrillator implants: results from the National Cardiovascular Data Registry. Circulation 2014;130(13):1037–1043. https://doi.org/10.1161/CIRCULATIONAHA.114.009081.
12. Dai M, Cai C, Vaibhav V, Sohail MR, Hayes DL, Hodge DO, et al. Trends of Cardiovascular Implantable Electronic Device Infection in 3 Decades: A Population-Based Study. JACC Clin Electrophysiol 2019;5(9):1071–1080. https://doi.org/10.1016/j.jacep.2019.06.016.
13. Tarakji KG, Wazni OM, Harb S, Hsu A, Saliba W, Wilkoff BL. Risk factors for 1-year mortality among patients with cardiac implantable electronic device infection undergoing transvenous lead extraction: the impact of the infection type and the presence of vegetation on survival. Europace 2014;16(10):1490–1495. https://doi.org/10.1093/europace/euu147.
14. Gharamti A, Kanafani ZA. Vascular Graft Infections: An update. *Infect Dis Clin North Am* 2018;32(4):789–809. https://doi.org/10.1016/j.idc.2018.06.003.
15. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, et al. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001;345(20):1435–1443. https://doi.org/10.1056/NEJMoa012175.
16. Rogers JG, Pagani FD, Tatooles AJ, Bhat G, Slaughter MS, Birks EJ, et al. Intrapericardial Left Ventricular Assist Device for Advanced Heart Failure. N Engl J Med 2017;376(5):451–460. https://doi.org/10.1056/NEJMoa1602954.
17. Mehra MR, Goldstein DJ, Uriel N, Cleveland JC Jr, Yuzefpolskaya M, Salerno C, et al. Two-Year Outcomes with a Magnetically Levitated Cardiac Pump in Heart Failure. N Engl J Med 2018;378(15):1386–1395. https://doi.org/10.1056/NEJMoa1800866.
18. Kusne S, Mooney M, Danziger-Isakov L, Kaan A, Lund LH, Lyster H, et al. An ISHLT consensus document for prevention and management strategies for mechanical circulatory support infection. J Heart Lung Transplant 2017;36(10):1137–1153. https://doi.org/10.1016/j.healun.2017.06.007.

19. Kusne S, Staley L, Arabia F. Prevention and Infection Management in Mechanical Circulatory Support Device Recipients. Clin Infect Dis 2017;64(2):222–228. https://doi.org/10.1093/cid/ciw698.
20. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30(4):633–638. https://doi.org/10.1086/313753.
21. Cantoni V, Sollini M, Green R, Berchiolli R, Lazzeri E, Mannarino T, et al. Comprehensive meta-analysis on [18F] FDG PET/CT and radiolabelled leukocyte SPECT–SPECT/CT imaging in infectious endocarditis and cardiovascular implantable electronic device infections. Clin Transl Imaging 2018;6(3):3–18. https://doi.org/10.1007/s40336-018-0265-z.
22. San S, Ravis E, Tessonier L, Philip M, Cammilleri S, Lavagna F, et al. Prognostic Value of (18)F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Infective Endocarditis. J Am Coll Cardiol 2019; 74(8):1031–1040. https://doi.org/10.1016/j.jacc.2019.06.050.
23. Husmann L, Ledergerber B, Anagnostopoulos A, Stolzmann P, Sah BR, Burger IA, et al. The role of FDG PET/CT in therapy control of aortic graft infection. Eur J Nucl Med Mol Imaging 2018;45(11):1987–1997. https://doi.org/10.1007/s00259-018-4069-1.
24. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, et al. [2015 ESC Guidelines for the management of infective endocarditis]. Kardiol Pol 2015;73(11):963–1027. https://doi.org/10.5603/KP.2015.0227.
25. Blomström-Lundqvist C, Traykov V, Erba PA, Burri H, Nielsen JC, Bongiorni MG, et al. European Heart Rhythm Association (EHRA) international consensus document on how to prevent, diagnose, and treat cardiac implantable electronic device infections-endorsed by the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS), the Latin American Heart Rhythm Society (LAHRS), International Society for Cardiovascular Infectious Diseases (ISCVID), and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2020;41(21):2012–2032. https://doi.org/10.1093/eurheartj/ehaa010.
26. Erba PA, Lancellotti P, Vilacosta I, Gaemperli O, Rouzet F, Hacker M, et al. Recommendations on nuclear and multimodality imaging in IE and CIED infections. Eur J Nucl Med Mol Imaging 2018;45(10):1795–1815. https://doi.org/10.1007/s00259-018-4025-0.
27. Delgado V, Ajmone Marsan N, de Waha S, Bonaros N, Brida M, Burrie H, et al. 2023 ESC Guidelines for the management of endocarditis. Eur Heart J 2023; 44(39):3948–4042. https://doi.org/10.1093/eurheartj/ehad193.
28. Weisse AB, Khan MY. The relationship between new cardiac conduction defects and extension of valve infection in native valve endocarditis. Clin Cardiol 1990; 13(5):337–345. https://doi.org/10.1002/clc.4960130507.
29. Tattevin P, Watt G, Revest M, Arvieux C, Fournier PE. Update on blood culture-negative endocarditis. Med Mal Infect 2015;45(1-2):1–8. https://doi.org/10.1016/j.medmal.2014.11.003.
30. Fournier PE, Gouriet F, Casalta JP, et al. Blood culture-negative endocarditis: Improving the diagnostic yield using new diagnostic tools. Medicine (Baltimore) 2017;96(47):e8392 https://doi.org/10.1097/MD.0000000000008392.
31. Habib G, Badano L, Tribouilloy C, Vilacosta I, Zamorano JL, Galderisi M, et al. Recommendations for the practice of echocardiography in infective endocarditis. Eur J Echocardiogr 2010;11(2):202–219. https://doi.org/10.1093/ejechocard/jeq004.
32. Pettersson GB, Coselli JS, Hussain ST, Griffin B, Blackstone EH, Gordon SM, et al. The American Association for Thoracic Surgery (AATS) consensus guidelines: Surgical treatment of infective endocarditis: Executive summary. J Thorac Cardiovasc Surg 2017;153(6):1241–1258.e29. https://doi.org/10.1016/j.jtcvs.2016.09.093.
33. Baddour LM, Wilson WR, Bayer AS, Fowler VG Jr, Tleyjeh IM, Rybak MJ, et al. Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications: A Scientific Statement for Healthcare Professionals From the American Heart Association. Circulation 2015;132(15):1435–1486. https://doi.org/10.1161/CIR.0000000000000296.
34. Tarakji KG, Chan EJ, Cantillon DJ, Doonan AL, Hu T, Schmitt S, et al. Cardiac implantable electronic device infections: presentation, management, and patient outcomes. *Heart Rhythm* 2010;7(8):1043–1047. https://doi.org/10.1016/j.hrthm.2010.05.016.
35. Kusumoto FM, Schoenfeld MH, Wilkoff BL, Berul CI, Birgersdotter-Green UM, Carrillo R, et al. HRS expert consensus statement on cardiovascular implantable electronic device lead management and extraction. Heart Rhythm 2017; 14(12):e503–e551. https://doi.org/10.1016/j.hrthm.2017.09.001.
36. Smith PN, Vidaillet HJ, Hayes JJ, Wethington PJ, Stahl L, Hull M, et al. Infections with nonthoracotomy implantable cardioverter defibrillators: can these be prevented? Pacing Clin Electrophysiol 1998;21(1 Pt 1):42–55. https://doi.org/10.1111/j.1540-8159.1998.tb01060.x.
37. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Executive Summary: Surviving Sepsis Campaign: International Guidelines for the Management of Sepsis and Septic Shock 2021. Crit Care Med 2021; 49(11):1974–1982. https://doi.org/10.1097/CCM.0000000000005357.
38. Hussein AA, Baghdy Y, Wazni OM, Brunner MP, Kabbach G, Shao M, et al. Microbiology of Cardiac Implantable Electronic Device Infections. JACC Clin Electrophysiol 2016;2(4):498–505. https://doi.org/10.1016/j.jacep.2016.01.019.
39. Maskarinec SA, Thaden JT, Cyr DD, Ruffin F, Souli M, Fowler VG. The Risk of Cardiac Device-Related Infection in Bacteremic Patients Is Species Specific: Results of a 12-Year Prospective Cohort. Open Forum Infect Dis 2017;4(3):ofx132. https://doi.org/10.1093/ofid/ofx132.
40. Nakajima I, Narui R, Tokutake K, Norton CA, Stevenson WG, Richardson TD, et al. Staphylococcus bacteremia without evidence of cardiac implantable electronic device infection. Heart Rhythm 2021;18(5):752–759. https://doi.org/10.1016/j.hrthm.2020.12.011.
41. Lin AY, Saul T, Aldaas OM, Lupercio F, Ho G, Pollema T, et al. Early Versus Delayed Lead Extraction in Patients With Infected Cardiovascular Implantable Electronic Devices. JACC Clin Electrophysiol 2021;7(6):755–763. https://doi.org/10.1016/j.jacep.2020.11.003.
42. Shah P, Birk SE, Cooper LB, Psotka MA, Kirklin JK, Barnett SD, et al. Stroke and death risk in ventricular assist device patients varies by ISHLT infection category: An INTERMACS analysis. J Heart Lung Transplant 2019;38(7):721–730. https://doi.org/10.1016/j.healun.2019.02.006.
43. Alvarez PA, Sperry BW, Pérez AL, Yaranov DM, Randhawa V, Luthman J, et al. Implantable Cardioverter Defibrillators in Patients With Continuous Flow Left Ventricular Assist Devices: Utilization Patterns, Related Procedures, and Complications. J Am Heart Assoc 2019;8(14):e011813. https://doi.org/10.1161/JAHA.118.011813.
44. Aslam S, Xie R, Cowger J, Kirklin JK, Chu VH, Schueler S, et al. Bloodstream infections in mechanical circulatory support device recipients in the International Society of Heart and Lung Transplantation Mechanically Assisted Circulation Support Registry: Epidemiology, risk factors, and mortality. J Heart Lung Transplant 2018;37(8):1013–1020. https://doi.org/10.1016/j.healun.2018.04.006.
45. Orvin K, Goldberg E, Bernstine H, Groshar D, Sagie A, Kornowski R, et al. The role of FDG-PET/CT imaging in early detection of extra-cardiac complications of infective endocarditis. Clin Microbiol Infect 2015;21(1):69–76. https://doi.org/10.1016/j.cmi.2014.08.012.
46. Pizzi MN, Roque A, Fernández-Hidalgo N, Cuéllar-Calabria H, Ferreira-González I, Gonzàlez-Alujas MT, et al. Improving the Diagnosis of Infective Endocarditis in Prosthetic Valves and Intracardiac Devices With 18F-Fluordeoxyglucose Positron Emission Tomography/Computed Tomography Angiography: Initial Results at an Infective Endocarditis Referral Center. Circulation 2015; 132(12):1113–1126. https://doi.org/10.1161/CIRCULATIONAHA.115.015316.
47. Gaynor SL, Zierer A, Lawton JS, Gleva MJ, Damiano RJ, Moon MR. Laser assistance for extraction of chronically implanted endocardial leads: infectious versus noninfectious indications. Pacing Clin Electrophysiol 2006;29(12):1352–1358. https://doi.org/10.1111/j.1540-8159.2006.00547.x.
48. Panagides V, Del Val D, Abdel-Wahab M, Mangner N, Durand E, Ihlemann N, et al. Perivalvular Extension of Infective Endocarditis After Transcatheter Aortic Valve Replacement. Clin Infect Dis 2022;75(4):638–646. https://doi.org/10.1093/cid/ciab1004.
49. Nowosielecka D, Jachec W, Polewczyk A, Tułecki Ł, Tomków K, Stefańczyk P, et al. Transesophageal echocardiography as a monitoring tool during transvenous lead extraction-does it improve procedure effectiveness? J Clin Med 2020(5):9. https://doi.org/10.3390/jcm9051382.
50. Sadek MM, Cooper JM, Frankel DS, et al. Utility of intracardiac echocardiography during transvenous lead extraction. Heart Rhythm 2017;14(12):1779–1785. https://doi.org/10.1016/j.hrthm.2017.08.023.
51. Shively BK, Gurule FT, Roldan CA, Leggett JH, Schiller NB. Diagnostic value of transesophageal compared with transthoracic echocardiography in infective endocarditis. J Am Coll Cardiol 1991;18(2):391–397. https://doi.org/10.1016/0735-1097(91)90591-v.
52. Daniel WG, Mugge A, Grote J, Hausmann D, Nikutta P, Laas J, et al. Comparison of transthoracic and transesophageal echocardiography for detection of abnormalities of prosthetic and bioprosthetic valves in the mitral and aortic positions. Am J Cardiol 1993;71(2):210–215. https://doi.org/10.1016/0002-9149(93)90740-4.
53. Jain V, Wang TKM, Bansal A, Farwati M, Gad M, Montane B, et al. Diagnostic performance of cardiac computed tomography versus transesophageal echocardiography in infective endocarditis: A contemporary comparative meta-analysis. J Cardiovasc Comput Tomogr 2021;15(4):313–321. https://doi.org/10.1016/j.jcct.2020.11.008.
54. Reynolds HR, Jagen MA, Tunick PA, Kronzon I. Sensitivity of transthoracic versus transesophageal echocardiography for the detection of native valve vegetations in the modern era. J Am Soc Echocardiogr 2003;16(1):67–70. https://doi.org/10.1067/mje.2003.43.
55. Jassal DS, Aminbakhsh A, Fang T, Shaikh N, Embil JM, Mackenzie GS, et al. Diagnostic value of harmonic transthoracic echocardiography in native valve infective endocarditis: comparison with transesophageal echocardiography. Cardiovasc Ultrasound 2007;5:20. https://doi.org/10.1186/1476-7120-5-20.
56. Casella F, Rana B, Casazza G, Bhan A, Kapetanakis S, Omigie J, et al. The potential impact of contemporary transthoracic echocardiography on the management of patients with native valve endocarditis: a comparison with transesophageal echocardiography. Echocardiography 2009;26(8):900–906. https://doi.org/10.1111/j.1540-8175.2009.00906.x.
57. Kini V, Logani S, Ky B, Chirinos JA, Ferrari VA, St John Sutton MG, et al. Transthoracic and transesophageal echocardiography for the indication of suspected infective endocarditis: vegetations, blood cultures and imaging. J Am Soc Echocardiogr 2010;23(4):396–402. https://doi.org/10.1016/j.echo.2009.12.017.
58. Klug D, Lacroix D, Savoye C, Goullard L, Grandmougin D, Hennequin JL, et al. Systemic infection related to endocarditis on pacemaker leads: clinical presentation and management. Circulation 1997;95(8):2098–2107. https://doi.org/10.1161/01.cir.95.8.2098.
59. Victor F, De Place C, Camus C, Le Breton H, Leclercq C, Pavin D, et al. Pacemaker lead infection: echocardiographic features, management, and outcome. Heart 1999;81(1):82–87. https://doi.org/10.1136/hrt.81.1.82.

60. Cacoub P, Leprince P, Nataf P, Hausfater P, Dorent R, Wechsler B, et al. Pacemaker infective endocarditis. Am J Cardiol 1998;82(4):480–484. https://doi.org/10.1016/s0002-9149(98)00365-8.
61. Abdelghani M, Nassif M, Blom NA, Van Mourik MS, Straver B, Koolbergen DR, et al. Infective Endocarditis After Melody Valve Implantation in the Pulmonary Position: A Systematic Review. J Am Heart Assoc 2018;7(13). https://doi.org/10.1161/JAHA.117.008163.
62. Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, et al. Recommendations for Noninvasive Evaluation of Native Valvular Regurgitation: A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance. J Am Soc Echocardiogr 2017;30(4):303–371. https://doi.org/10.1016/j.echo.2017.01.007.
63. Zoghbi WA, Asch FM, Bruce C, Gillam LD, Grayburn PA, Hahn RT, et al. Guidelines for the Evaluation of Valvular Regurgitation After Percutaneous Valve Repair or Replacement: A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Angiography and Interventions, Japanese Society of Echocardiography, and Society for Cardiovascular Magnetic Resonance. J Am Soc Echocardiogr 2019;32(4):431–475. https://doi.org/10.1016/j.echo.2019.01.003.
64. Zoghbi WA, Chambers JB, Dumesnil JG, Foster E, Gottdiener JS, Grayburn PA, et al. Recommendations for evaluation of prosthetic valves with echocardiography and doppler ultrasound: a report From the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. J Am Soc Echocardiogr 2009;22(9):975–1014. https://doi.org/10.1016/j.echo.2009.07.013. quiz 1082-4.
65. Lang RM, Badano LP, Tsang W, Adams DH, Agricola E, Buck T, et al. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. J Am Soc Echocardiogr 2012;25(1):3–46. https://doi.org/10.1016/j.echo.2011.11.010.
66. Berdejo J, Shibayama K, Harada K, Tanaka J, Mihara H, Gurudevan SV, et al. Evaluation of vegetation size and its relationship with embolism in infective endocarditis: a real-time 3-dimensional transesophageal echocardiography study. Circ Cardiovasc Imaging 2014;7(1):149–154. https://doi.org/10.1161/CIRCIMAGING.113.000938.
67. Mohananey D, Mohadjer A, Pettersson G, Navia J, Gordon S, Shrestha N, et al. Association of Vegetation Size With Embolic Risk in Patients With Infective Endocarditis: A Systematic Review and Meta-analysis. JAMA Intern Med 2018;178(4):502–510. https://doi.org/10.1001/jamainternmed.2017.8653.
68. Salaun E, Sportouch L, Barral PA, Hubert S, Lavoute C, Casalta AC, et al. Diagnosis of Infective Endocarditis After TAVR: Value of a Multimodality Imaging Approach. JACC Cardiovasc Imaging 2018;11(1):143–146. https://doi.org/10.1016/j.jcmg.2017.05.016.
69. Mangner N, Woitek F, Haussig S, Schlotter F, Stachel G, Höllriegel R, et al. Incidence, Predictors, and Outcome of Patients Developing Infective Endocarditis Following Transfemoral Transcatheter Aortic Valve Replacement. J Am Coll Cardiol 2016;67(24):2907–2908. https://doi.org/10.1016/j.jacc.2016.03.588.
70. Fowler VG, Li J, Corey GR, Boley J, Marr KA, Gopal AK, et al. Role of echocardiography in evaluation of patients with Staphylococcus aureus bacteremia: experience in 103 patients. J Am Coll Cardiol 1997;30(4):1072–1078. https://doi.org/10.1016/s0735-1097(97)00250-7.
71. Leccisotti L, Perna F, Lago M, Leo M, Stefanelli A, Calcagni ML, et al. Cardiovascular implantable electronic device infection: delayed vs standard FDG PET-CT imaging. J Nucl Cardiol 2014;21(3):622–632. https://doi.org/10.1007/s12350-014-9896-2.
72. Duval X, Selton-Suty C, Alla F, Salvador-Mazenq M, Bernard Y, Weber M, et al. Endocarditis in patients with a permanent pacemaker: a 1-year epidemiological survey on infective endocarditis due to valvular and/or pacemaker infection. Clin Infect Dis 2004;39(1):68–74. https://doi.org/10.1086/421493.
73. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR, et al. Infective endocarditis complicating permanent pacemaker and implantable cardioverter-defibrillator infection. Mayo Clin Proc 2008;83(1):46–53. https://doi.org/10.4065/83.1.46.
74. Thyagarajan B, Kumar MP, Sikachi RR, Agrawal A. Endocarditis in left ventricular assist device. Intractable Rare Dis Res 2016;5(3):177–184. https://doi.org/10.5582/irdr.2016.01049.
75. Stainback RF, Estep JD, Agler DA, Birks EJ, Bremer M, Hung J, et al. Echocardiography in the Management of Patients with Left Ventricular Assist Devices: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr 2015;28(8):853–909. https://doi.org/10.1016/j.echo.2015.05.008.
76. Horgan SJ, Mediratta A, Gillam LD. Cardiovascular Imaging in Infective Endocarditis: A Multimodality Approach. Circ Cardiovasc Imaging 2020;13(7):e008956 https://doi.org/10.1161/CIRCIMAGING.120.008956.
77. Knol WG, Wahadat AR, Roos-Hesselink JW, Van Mieghem NM, Tanis W, Bogers AJJC, et al. Screening for coronary artery disease in early surgical treatment of acute aortic valve infective endocarditis. Interact Cardiovasc Thorac Surg 2021;32(4):522–529. https://doi.org/10.1093/icvts/ivaa313.
78. Faure ME, Swart LE, Dijkshoorn ML, Bekkers JA, van Straten M, Nieman K, et al. Advanced CT acquisition protocol with a third-generation dual-source CT scanner and iterative reconstruction technique for comprehensive prosthetic heart valve assessment. Eur Radiol 2018;28(5):2159–2168. https://doi.org/10.1007/s00330-017-5163-7.
79. Saeedan MB, Wang TKM, Cremer P, Wahadat AR, Budde RPJ, Unai S, et al. Role of Cardiac CT in Infective Endocarditis: Current Evidence, Opportunities, and Challenges. Radiol Cardiothorac Imaging 2021;3(1):e200378. https://doi.org/10.1148/ryct.2021200378.
80. Feuchtner GM, Stolzmann P, Dichtl W, Schertler T, Bonatti J, Scheffel H, et al. Multislice computed tomography in infective endocarditis: comparison with transesophageal echocardiography and intraoperative findings. J Am Coll Cardiol 2009;53(5):436–444. https://doi.org/10.1016/j.jacc.2008.01.077.
81. Jing L, Song Y. Comparing the diagnostic accuracy of computed tomography vs transoesophageal echocardiography for infective endocarditis - A meta-analysis. Pak J Med Sci 2022;38(3Part-I):736–742. https://doi.org/10.12669/pjms.38.3.5139.
82. de Vries EF, Roca M, Jamar F, Israel O, Signore A. Guidelines for the labelling of leucocytes with (99m)Tc-HMPAO. Inflammation/Infection Taskgroup of the European Association of Nuclear Medicine. Eur J Nucl Med Mol Imaging 2010;37(4):842–848. https://doi.org/10.1007/s00259-010-1394-4.
83. Roca M, de Vries EF, Jamar F, Israel O, Signore A. Guidelines for the labelling of leucocytes with (111)In-oxine. Inflammation/Infection Taskgroup of the European Association of Nuclear Medicine. Eur J Nucl Med Mol Imaging 2010;37(4):835–841. https://doi.org/10.1007/s00259-010-1393-5.
84. Erba PA, Glaudemans AW, Veltman NC, Sollini M, Pacilio M, Galli F, et al. Image acquisition and interpretation criteria for 99mTc-HMPAO-labelled white blood cell scintigraphy: results of a multicentre study. Eur J Nucl Med Mol Imaging 2014;41(4):615–623. https://doi.org/10.1007/s00259-013-2631-4.
85. Erba PA, Conti U, Lazzeri E, Sollini M, Doria R, De Tommasi SM, et al. Added value of 99mTc-HMPAO-labeled leukocyte SPECT/CT in the characterization and management of patients with infectious endocarditis. J Nucl Med 2012;53(8):1235–1243. https://doi.org/10.2967/jnumed.111.099424.
86. Hyafil F, Rouzet F, Lepage L, Benali K, Raffoul R, Duval X, et al. Role of radiolabelled leucocyte scintigraphy in patients with a suspicion of prosthetic valve endocarditis and inconclusive echocardiography. Eur Heart J Cardiovasc Imaging 2013;14(6):586–594. https://doi.org/10.1093/ehjci/jet029.
87. Rouzet F, Chequer R, Benali K, Lepage L, Ghodbane W, Duval X, et al. Respective performance of 18F-FDG PET and radiolabeled leukocyte scintigraphy for the diagnosis of prosthetic valve endocarditis. J Nucl Med 2014;55(12):1980–1985. https://doi.org/10.2967/jnumed.114.141895.
88. Erba PA, Sollini M, Conti U, Bandera F, Tascini C, De Tommasi SM, et al. Radiolabeled WBC scintigraphy in the diagnostic workup of patients with suspected device-related infections. JACC Cardiovasc Imaging 2013;6(10):1075–1086. https://doi.org/10.1016/j.jcmg.2013.08.001.
89. Calais J, Touati A, Grall N, Laouénan C, Benali K, Mahida B, et al. Diagnostic impact of 18F-Fluorodeoxyglucose positron emission tomography/computed tomography and white blood cell SPECT/computed tomography in patients with suspected cardiac implantable electronic device chronic infection. Circ Cardiovasc Imaging 2019;12(7):e007188 https://doi.org/10.1161/CIRCIMAGING.117.007188.
90. de Vaugelade C, Mesguich C, Nubret K, Camou F, Greib C, Dournes G, et al. Infections in patients using ventricular-assist devices: Comparison of the diagnostic performance of ^{18}F-FDG PET/CT scan and leucocyte-labeled scintigraphy. J Nucl Cardiol 2019;26(1):42–55. https://doi.org/10.1007/s12350-018-1323-7.
91. Erba PA, Leo G, Sollini M, Tascini C, Boni R, Berchiolli RN, et al. Radiolabelled leucocyte scintigraphy versus conventional radiological imaging for the management of late, low-grade vascular prosthesis infections. Eur J Nucl Med Mol Imaging 2014;41(2):357–368. https://doi.org/10.1007/s00259-013-2582-9.
92. Sacks D, Baxter B, Campbell BCV, Carpenter JS, Cognard C, Dippel D, et al. Multisociety consensus quality improvement revised consensus statement for endovascular therapy of acute ischemic stroke. Int J Stroke 2018;13(6):612–632. https://doi.org/10.1177/1747493018778713.
93. Fu Y, Maianu L, Melbert BR, Garvey WT. Facilitative glucose transporter gene expression in human lymphocytes, monocytes, and macrophages: a role for GLUT isoforms 1, 3, and 5 in the immune response and foam cell formation. Blood Cells Mol Dis 2004;32(1):182–190. https://doi.org/10.1016/j.bcmd.2003.09.002.
94. Palestro CJ, Brandon D, Dibble EH, Keidar Z, Kwak J. FDG PET in Evaluation of Patients With Fever of Unknown Origin: AJR Expert Panel Narrative Review. AJR Am J Roentgenol 2023; https://doi.org/10.2214/AJR.22.28726.
95. Dilsizian V, Bacharach SL, Beanlands RS, Bergmann SR, Delbeke D, Dorbala S, et al. ASNC imaging guidelines/SNMMI procedure standard for positron emission tomography (PET) nuclear cardiology procedures. J Nucl Cardiol 2016;23(5):1187–1226. https://doi.org/10.1007/s12350-016-0522-3.
96. Christopoulos G, Jouni H, Acharya GA, Blauwet LA, Kapa S, Bois J, et al. Suppressing physiologic 18-fluorodeoxyglucose uptake in patients undergoing positron emission tomography for cardiac sarcoidosis: The effect of a structured patient preparation protocol. J Nucl Cardiol 2021;28(2):661–671. https://doi.org/10.1007/s12350-019-01746-4.
97. Boursier C, Duval X, Bourdon A, Imbert L, Mahida B, Chevalier E, et al. ECG-Gated Cardiac FDG PET Acquisitions Significantly Improve Detectability of Infective Endocarditis. JACC Cardiovasc Imaging 2020;13(12):2691–2693. https://doi.org/10.1016/j.jcmg.2020.06.036.

98. Al-Mallah MH, Bateman TM, Branch KR, Crean A, Gingold EL, Thompson RC, et al. ASNC/AAPM/SCCT/SNMMI guideline for the use of CT in hybrid nuclear/CT cardiac imaging. J Nucl Cardiol 2022; https://doi.org/10.1007/s12350-022-03089-z.
99. Roque A, Pizzi MN, Fernández-Hidalgo N, Romero-Farina G, Burcet G, Reyes-Juarez JL, et al. The valve uptake index: improving assessment of prosthetic valve endocarditis and updating [18F]FDG PET/CT(A) imaging criteria. Eur Heart J Cardiovasc Imaging 2022;23(9):1260–1271. https://doi.org/10.1093/ehjci/-jeab279.
100. Bourque JM, Einstein AJ, Dorbala S. ASNC Imaging Indications (ASNC-I2): Multisocietal indications for radionuclide imaging in the multimodality context-Series rationale and methodology. J Nucl Cardiol 2022;29(5):2667–2678. https://doi.org/10.1007/s12350-021-02800-w.
101. Hendel RC, Patel MR, Allen JM, Min JK, Shaw LJ, Wolk MJ, et al. Appropriate use of cardiovascular technology: 2013 ACCF appropriate use criteria methodology update: a report of the American College of Cardiology Foundation appropriate use criteria task force. J Am Coll Cardiol 2013;61(12):1305–1317. https://doi.org/10.1016/j.jacc.2013.01.025.
102. Dorbala S, Ando Y, Bokhari S, Dispenzieri A, Falk RH, Ferrari VA, et al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis: Part 1 of 2-evidence base and standardized methods of imaging. J Nucl Cardiol 2019;26(6):2065–2123. https://doi.org/10.1007/s12350-019-01760-6.
103. Fitch K, Bernstein SJ, Aguilar MD, Burnand B, LaCalle JR, Lazaro P, et al. The Rand/UCLA appropriateness method user's manual. Rand; 2001. p. 109. xiii. Available at https://apps.dtic.mil/sti/citations/ADA393235.
104. Wolk MJ, Bailey SR, Doherty JU, Douglas PS, Hendel RC, Kramer CM, et al. ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 multimodality appropriate use criteria for the detection and risk assessment of stable ischemic heart disease: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. J Am Coll Cardiol 2014;63(4):380–406. https://doi.org/10.1016/j.-jacc.2013.11.009.
105. Bonow RO, Brown AS, Gillam LD, Kapadia SR, Kavinsky CJ, Lindman BR, et al. ACC/AATS/AHA/ASE/EACTS/HVS/SCA/SCAI/SCCT/SCMR/STS 2017 Appropriate Use Criteria for the Treatment of Patients With Severe Aortic Stenosis: A Report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, European Association for Cardio-Thoracic Surgery, Heart Valve Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. J Am Soc Echocardiogr 2018;31(2):117–147. https://doi.org/10.1016/j.echo.2017.10.020.
106. Patel MR, Spertus JA, Brindis RG, Hendel RC, Douglas PS, Peterson ED, et al. ACCF proposed method for evaluating the appropriateness of cardiovascular imaging. J Am Coll Cardiol 2005;46(8):1606–1613. https://doi.org/10.1016/j.-jacc.2005.08.030.
107. Brook RH, Chassin MR, Fink A, Solomon DH, Kosecoff J, Park RE. A method for the detailed assessment of the appropriateness of medical technologies. Int J Technol Assess Health Care 1986;2(1):53–63. https://doi.org/10.1017/s0266462300002774.
108. Patel KK, Spertus JA, Chan PS, Sperry BW, Thompson RC, Al Badarin F, et al. Extent of Myocardial Ischemia on Positron Emission Tomography and Survival Benefit With Early Revascularization. J Am Coll Cardiol 2019;74(13):1645–1654. https://doi.org/10.1016/j.jacc.2019.07.055.
109. Doherty JU, Kort S, Mehran R, Schoenhagen P, Soman P. ACC/AATS/AHA/ASE/ASNC/HRS/SCAI/SCCT/SCMR/STS 2017 Appropriate Use Criteria for Multimodality Imaging in Valvular Heart Disease: A Report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. J Am Coll Cardiol 2017;70(13):1647–1672. https://doi.org/10.1016/j.jacc.2017.07.732.
110. Patel MR, White RD, Abbara S, Bluemke DA, Herfkens RJ, Picard M, et al. ACCF/ACR/ASE/ASNC/SCCT/SCMR appropriate utilization of cardiovascular imaging in heart failure: a joint report of the American College of Radiology Appropriateness Criteria Committee and the American College of Cardiology Foundation Appropriate Use Criteria Task Force. J Am Coll Cardiol 2013;61(21):2207–2231. https://doi.org/10.1016/j.jacc.2013.02.005.
111. Bernstein SJ, Hofer TP, Meijler AP, Rigter H. Setting standards for effectiveness: a comparison of expert panels and decision analysis. Int J Qual Health Care 1997;9(4):255–263. https://doi.org/10.1093/intqhc/9.4.255.
112. Kuntz KM, Tsevat J, Weinstein MC, Goldman L. Expert panel vs decision-analysis recommendations for postdischarge coronary angiography after myocardial infarction. JAMA 1999;282(23):2246–2251. https://doi.org/10.1001/jama.282.23.2246.
113. PETERSDORF RG, BEESON PB. Fever of unexplained origin: report on 100 cases. Medicine (Baltimore) 1961;40:1–30. https://doi.org/10.1097/00005792-196102000-00001.
114. Geraci JE, Wilson WR. Symposium on infective endocarditis. III. Endocarditis due to gram-negative bacteria. Report of 56 cases. Mayo Clin Proc 1982;57(3):145–148.
115. Ribeyrolles S, Ternacle J, San S, Lepeule R, Moussafeur A, Faivre L, et al. Infective endocarditis without biological inflammatory syndrome: Description of a particular entity. Arch Cardiovasc Dis 2019;112(6-7):381–389. https://doi.org/10.1016/-j.acvd.2019.02.005.
116. Hannan MM, Husain S, Mattner F, Danziger-Isakov L, Drew RJ, Corey GR, et al. Working formulation for the standardization of definitions of infections in patients using ventricular assist devices. J Heart Lung Transplant 2011;30(4):375–384. https://doi.org/10.1016/j.healun.2011.01.717.
117. Pelletier-Galarneau M, Abikhzer G, Harel F, Dilsizian V. Detection of Native and Prosthetic Valve Endocarditis: Incremental Attributes of Functional FDG PET/CT over Morphologic Imaging. Curr Cardiol Rep 2020;22(9):93. https://doi.org/10.1007/s11886-020-01334-w.
118. Erba PA, Pizzi MN, Roque A, Salaun E, Lancellotti P, Tornos P, et al. Multimodality imaging in infective endocarditis: An imaging team within the endocarditis team. Circulation 2019;140(21):1753–1765. https://doi.org/10.1161/CIRCULATIONAHA.119.040228.
119. Abikhzer G, Martineau P, Grégoire J, Finnerty V, Harel F, Pelletier-Galarneau M. 18F-FDG-PET CT for the evaluation of native valve endocarditis. J Nucl Cardiol 2022;29(1):158–165. https://doi.org/10.1007/s12350-020-02092-6.
120. Wang TKM, Sanchez-Nadales A, Igbinomwanhia E, Cremer P, Griffin B, Xu B. Diagnosis of Infective Endocarditis by Subtype Using (18)F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography: A Contemporary Meta-Analysis. Circ Cardiovasc Imaging 2020;13(6):e010600. https://doi.org/10.1161/-CIRCIMAGING.120.010600.
121. Hitzenbichler F, Joha T, Simon M, Grosse J, Menhart K, Hellwig D, et al. Candida Endocarditis in Patients with Candidemia: A Single-Center Experience of 14 Cases. Mycopathologia 2020;185(6):1057–1067. https://doi.org/10.1007/s11046-020-00492-3.
122. Pijl JP, Londema M, Kwee TC, Nijsten MWN, Slart RHJA, Dierckx RAJO, et al. FDG-PET/CT in intensive care patients with bloodstream infection. Crit Care 2021;25(1):133. https://doi.org/10.1186/s13054-021-03557-x.
123. Dahl A, Hernandez-Meneses M, Perissinotti A, Vidal B, Quintana E, Miro JM. Echocardiography and FDG-PET/CT scan in Gram-negative bacteremia and cardiovascular infections. Curr Opin Infect Dis 2021;34(6):728–736. https://doi.org/10.1097/QCO.0000000000000781.
124. Bae SW. Positron Emission Tomography with Computed Tomography in Evaluations of Classical Fever of Unknown Origin and Length of Hospitalization: A 10-Year Medical Record Review of a Tertiary Hospital. Infect Chemother 2022; https://doi.org/10.3947/ic.2022.0082.
125. Wright WF, Auwaerter PG, Dibble EH, Rowe SP, Mackowiak PA. Imaging a Fever-Redefining the Role of 2-deoxy-2-[18F]Fluoro-D-Glucose-Positron Emission Tomography/Computed Tomography in Fever of Unknown Origin Investigations. Clin Infect Dis 2021;72(7):1279–1286. https://doi.org/10.1093/cid/ciaa1220.
126. Bleeker-Rovers CP, de Kleijn EM, Corstens FH, van der Meer JW, Oyen WJ. Clinical value of FDG PET in patients with fever of unknown origin and patients suspected of focal infection or inflammation. Eur J Nucl Med Mol Imaging 2004;31(1):29–37. https://doi.org/10.1007/s00259-003-1338-3.
127. Anton-Vazquez V, Cannata A, Amin-Youssef G, Watson S, Fife A, Mulholland N, et al. Diagnostic value of 18F-FDG PET/CT in infective endocarditis. Clin Res Cardiol 2022;111(6):673–679. https://doi.org/10.1007/s00392-021-01975-z.
128. Mikail N, Benali K, Mahida B, Vigne J, Hyafil F, Rouzet F, et al. F-FDG-PET/CT Imaging to Diagnose Septic Emboli and Mycotic Aneurysms in Patients with Endocarditis and Cardiac Device Infections. Curr Cardiol Rep 2018;20(3):14. https://doi.org/10.1007/s11886-018-0956-0.
129. Duval X, Iung B. Extracardiac Imaging of Infective Endocarditis. Curr Infect Dis Rep 2017;19(7):24. https://doi.org/10.1007/s11908-017-0580-y.
130. Holcman K, Rubiś P, Stępień A, Graczyk K, Podolec P, Kostkiewicz M. The Diagnostic Value of 99mTc-HMPAO-Labelled White Blood Cell Scintigraphy and 18F-FDG PET/CT in Cardiac Device-Related Infective Endocarditis-A Systematic Review. J Pers Med 2021(10):11. https://doi.org/10.3390/jpm11101016.
131. Caobelli F, Wollenweber T, Bavendiek U, Kühn C, Schütze C, Geworski L, et al. Simultaneous dual-isotope solid-state detector SPECT for improved tracking of white blood cells in suspected endocarditis. Eur Heart J 2017;38(6):436–443. https://doi.org/10.1093/eurheartj/ehw231.
132. Galea N, Bandera F, Lauri C, Autore C, Laghi A, Erba PA. Multimodality Imaging in the Diagnostic Work-Up of Endocarditis and Cardiac Implantable Electronic Device (CIED) Infection. J Clin Med 2020;14(7):9. https://doi.org/10.3390/jcm9072237.
133. Swart LE, Gomes A, Scholtens AM, Sinha B, Tanis W, Lam MGEH, et al. Improving the Diagnostic Performance of 18F-Fluorodeoxyglucose Positron-Emission Tomography/Computed Tomography in Prosthetic Heart Valve Endocarditis. Circulation 2018;138(14):1412–1427. https://doi.org/10.1161/CIRCULATIONAHA.118.035032.
134. Wahadat AR, Tanis W, Swart LE, Scholtens A, Krestin GP, van Mieghem NMDA, et al. Added value of (18)F-FDG-PET/CT and cardiac CTA in suspected transcatheter aortic valve endocarditis. J Nucl Cardiol 2021;28(5):2072–2082. https://doi.org/10.1007/s12350-019-01963-x.
135. Erba PA, Israel O. SPECT/CT in infection and inflammation. Clin Transl Imaging 2014;2:519–535.
136. Holcman K, Szot W, Rubiś P, Leśniak-Sobelga A, Hlawaty M, Wiśniowska-Śmiałek S, et al. 99mTc-HMPAO-labeled leukocyte SPECT/CT and transthoracic

echocardiography diagnostic value in infective endocarditis. Int J Cardiovasc Imaging 2019;35(4):749–758. https://doi.org/10.1007/s10554-018-1487-x.
137. Juneau D, Golfam M, Hazra S, Zuckier LS, Garas S, Redpath C, et al. Positron emission tomography and single-photon emission computed tomography imaging in the diagnosis of cardiac implantable electronic device infection: A systematic review and meta-analysis. Circ Cardiovasc Imaging 2017;10(4) https://doi.org/10.1161/CIRCIMAGING.116.005772.
138. Ruiz-Zafra J, Rodríguez-Fernández A, Sánchez-Palencia A, Cueto A. Surgical adhesive may cause false positives in integrated positron emission tomography and computed tomography after lung cancer resection. Eur J Cardiothorac Surg 2013;43(6):1251–1253. https://doi.org/10.1093/ejcts/ezs643.
139. Ishikita A, Sakamoto I, Yamamura K, Umemoto S, Nagata H, Kitamura Y, et al. Usefulness of (18)F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in the Diagnosis of Infective Endocarditis in Patients With Adult Congenital Heart Disease. Circ J 2021;85(9):1505–1513. https://doi.org/10.1253/circj.CJ-20-1067.
140. Kim J, Feller ED, Chen W, Liang Y, Dilsizian V. FDG PET/CT for Early Detection and Localization of Left Ventricular Assist Device Infection: Impact on Patient Management and Outcome. JACC Cardiovasc Imaging 2019;12(4):722–729. https://doi.org/10.1016/j.jcmg.2018.01.024.
141. Mahmood M, Kendi AT, Ajmal S, Farid S, O'Horo JC, Chareonthaitawee P, et al. Meta-analysis of 18F-FDG PET/CT in the diagnosis of infective endocarditis. J Nucl Cardiol 2019;26(3):922–935. https://doi.org/10.1007/s12350-017-1092-8.
142. Albano D, Dondi F, Gazzilli M, Giubbini R, Bertagna F. Meta-Analysis of the Diagnostic Performance of 18F-FDG-PET/CT Imaging in Native Valve Endocarditis. JACC Cardiovasc Imaging 2021;14(5):1063–1065. https://doi.org/10.1016/j.jcmg.2020.09.021.
143. Kamani CH, Allenbach G, Jreige M, Pavon AG, Meyer M, Testart N, et al. Diagnostic Performance of 18F-FDG PET/CT in Native Valve Endocarditis: Systematic Review and Bivariate Meta-Analysis. Diagnostics (Basel) 2020;10(10) https://doi.org/10.3390/diagnostics10100754.
144. Gomes A, Glaudemans AWJM, Touw DJ, van Melle JP, Willems TP, Maass AH, et al. Diagnostic value of imaging in infective endocarditis: a systematic review. Lancet Infect Dis 2017;17(1):e1–e14. https://doi.org/10.1016/S1473-3099(16)30141-4.
145. Ten Hove D, Treglia G, Slart RHJA, Damman K, Wouthuyzen-Bakker M, Postma DF, et al. The value of 18F-FDG PET/CT for the diagnosis of device-related infections in patients with a left ventricular assist device: a systematic review and meta-analysis. Eur J Nucl Med Mol Imaging 2021;48(1):241–253. https://doi.org/10.1007/s00259-020-04930-8.
146. Tam MC, Patel VN, Weinberg RL, Hulten EA, Aaronson KD, Pagani FD, et al. Diagnostic accuracy of FDG PET/CT in suspected LVAD infections: A case series, systematic review, and meta-analysis. JACC Cardiovasc Imaging 2020;13(5):1191–1202. https://doi.org/10.1016/j.jcmg.2019.04.024.
147. Sommerlath Sohns JM, Kröhn H, Schöde A, Derlin T, Haverich A, Schmitto JD, et al. 18F-FDG PET/CT in left-ventricular assist device infection: Initial results supporting the usefulness of image-guided therapy. J Nucl Med 2020;61(7):971–976. https://doi.org/10.2967/jnumed.119.237628.
148. Roque A, Pizzi MN, Fernandez-Hidalgo N, Permanyer E, Cuellar-Calabria H, Romero-Farina G, et al. Morpho-metabolic post-surgical patterns of non-infected prosthetic heart valves by [18F]FDG PET/CTA: "normality" is a possible diagnosis. Eur Heart J Cardiovasc Imaging 2020;21(1):24–33. https://doi.org/10.1093/ehjci/jez222.
149. Slart RHJA, Glaudemans AWJM, Gheysens O, Lubberink M, Kero T, Dweck MR, et al. Procedural recommendations of cardiac PET/CT imaging: standardization in inflammatory-, infective-, infiltrative-, and innervation (4Is)-related cardiovascular diseases: a joint collaboration of the EACVI and the EANM. Eur J Nucl Med Mol Imaging 2021;48(4):1016–1039. https://doi.org/10.1007/s00259-020-05066-5.
150. Dilsizian V, Budde RPJ, Chen W, Mankad SV, Lindner JR, Nieman K. Best Practices for Imaging Cardiac Device-Related Infections and Endocarditis: A JACC: Cardiovascular Imaging Expert Panel Statement. JACC Cardiovasc Imaging 2022;15(5):891–911. https://doi.org/10.1016/j.jcmg.2021.09.029.
151. Chen W, Sajadi MM, Dilsizian V. Merits of FDG PET/CT and functional molecular imaging over anatomic imaging with echocardiography and CT Angiography for the diagnosis of cardiac device infections. JACC Cardiovasc Imaging 2018;11(11):1679–1691. https://doi.org/10.1016/j.jcmg.2018.08.026.
152. Chen W, Dilsizian V. Is 18F-Flurodeoxyglucose positron emission tomography/computed tomography more reliable than clinical standard diagnosis for guiding patient management decisions in cardiac implantable electronic device infection? Circ Cardiovasc Imaging 2019;12(7):e009453. https://doi.org/10.1161/CIRCIMAGING.119.009453.
153. Chen W, Dilsizian V. Molecular imaging of cardiovascular device infection: Targeting the bacteria or the host-pathogen immune response? J Nucl Med 2020;61:319–326.
154. Litzler PY, Manrique A, Etienne M, Salles A, Edet-Sanson A, Vera P, et al. Leukocyte SPECT/CT for detecting infection of left-ventricular-assist devices: preliminary results. J Nucl Med 2010;51(7):1044–1048. https://doi.org/10.2967/jnumed.109.070664.
155. van Rijsewijk ND, Helthuis JHG, Glaudemans A, Wouthuyzen-Bakker M, Prakken NHJ, Liesker DJ, et al. Added Value of Abnormal Lymph Nodes Detected with FDG-PET/CT in Suspected Vascular Graft Infection. Biology (Basel) 2023;5(2):12. https://doi.org/10.3390/biology12020251.
156. Mathieu C, Mikaïl N, Benali K, Iung B, Duval X, Nataf P, et al. Characterization of 18F-Fluorodeoxyglucose Uptake Pattern in Noninfected Prosthetic Heart Valves. Circ Cardiovasc Imaging 2017;10(3):e005585. https://doi.org/10.1161/-CIRCIMAGING.116.005585.