Circulation

AHA SCIENTIFIC STATEMENT

Update on Cardiovascular Implantable Electronic Device Infections and Their Prevention, Diagnosis, and Management: A Scientific Statement From the American Heart Association

Endorsed by the International Society for Cardiovascular Infectious Diseases

Larry M. Baddour, MD, FAHA, Chair; Zerelda Esquer Garrigos, MD; M. Rizwan Sohail, MD; Eva Havers-Borgersen, MD; Andrew D. Krahn, MD; Vivian H. Chu, MD; Connie S. Radke, MSN, NP; Jennifer Avari-Silva, MD, FAHA; Mikhael F. El-Chami, MD; Jose M. Miro, MD, PhD; Daniel C. DeSimone, MD, Vice Chair; on behalf of the American Heart Association Council on Lifelong Congenital Heart Disease and Heart Health in the Young (Young Hearts); and Council on Clinical Cardiology

ABSTRACT: The American Heart Association sponsored the first iteration of a scientific statement that addressed all aspects of cardiovascular implantable electronic device infection in 2010. Major advances in the prevention, diagnosis, and management of these infections have occurred since then, necessitating a scientific statement update. An 11-member writing group was identified and included recognized experts in cardiology and infectious diseases, with a career focus on cardiovascular infections. The group initially met in October 2022 to develop a scientific statement that was drafted with front-line clinicians in mind and focused on providing updated clinical information to enhance outcomes of patients with cardiovascular implantable electronic device infection. The current scientific statement highlights recent advances in prevention, diagnosis, and management, and how they may be incorporated in the complex care of patients with cardiovascular implantable electronic device infection.

Key Words: AHA Scientific Statements ■ defibrillators, implantable ■ diagnosis ■ echocardiography, transesophageal ■ endocarditis ■ infection

Cardiovascular implantable electronic device infection (CIEDI) is life-threatening and often characterized by difficulties both in diagnosis and in complex patient management. Cardiovascular implantable electronic device (CIED)-related infective endocarditis (IE) frequently accounts for these difficulties. Moreover, 40-year trends data have demonstrated that patients with CIED-related IE are older with more comorbid conditions and have more complex cardiac devices.[1] Since publication of our initial version of a scientific statement in 2010,[2] important advances have been published that addressed CIEDI prevention, diagnosis, and management. These include (1) 2 randomized controlled trials (PADIT[3] [Prevention of Arrhythmia Device Infection Trial] and WRAP-IT[4] [Worldwide Randomized Antibiotic Envelope Infection Prevention Trial]) that evaluated CIEDI prevention measures, the latter of which included use of an antibiotic-impregnated envelope at the time of device placement; (2) investigations that reevaluated the role of transesophageal echocardiography and its diagnostic limitations in distinguishing infectious versus noninfectious CIED lead masses[5]; (3) advantages of fluorine-18-fludeoxyglucose positron emission tomography/computerized tomography scanning ([^{18}F]FDG PET/CT) in the diagnosis of CIEDI[6]; (4) the citation of CIED as a predisposition to the development of IE as a specific minor criterion in the updated 2023 Duke-International Society for Cardiovascular Infectious Diseases criteria for IE[7]; (5) evaluation of both prevention- and management-related studies and

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIR.0000000000001187

Circulation is available at www.ahajournals.org/journal/circ

the roles of novel devices, including leadless pacemakers (LPMs) and subcutaneous implantable cardioverter defibrillators (S-ICDs). Six infection risk scores[8] have been used to estimate the risk of developing CIEDI that may be useful in identifying potential candidates for incremental prevention measures, and alternate device platforms such as a LPM or S-ICD. In addition, these scores have been used to determine the use of the above-mentioned antibiotic-eluting envelope in CIEDI prevention; and (6) an evaluation of recently published experiences with percutaneous mechanical aspiration systems being used to remove right-sided vegetations complicating CIEDI in select cases.

This AHA scientific statement was developed by a robust and experienced writing group (WG) whose collective goal was to enhance outcomes in patients with CIEDI (Figure 1). It is not intended, however, to be comprehensive. Therefore, a review with detailed aspects of CIEDI, including clinical features, associated risk factors, incidence, epidemiology, and pathogenesis, was not conducted. Also, the AHA scientific statement is not a guideline and, therefore, did not

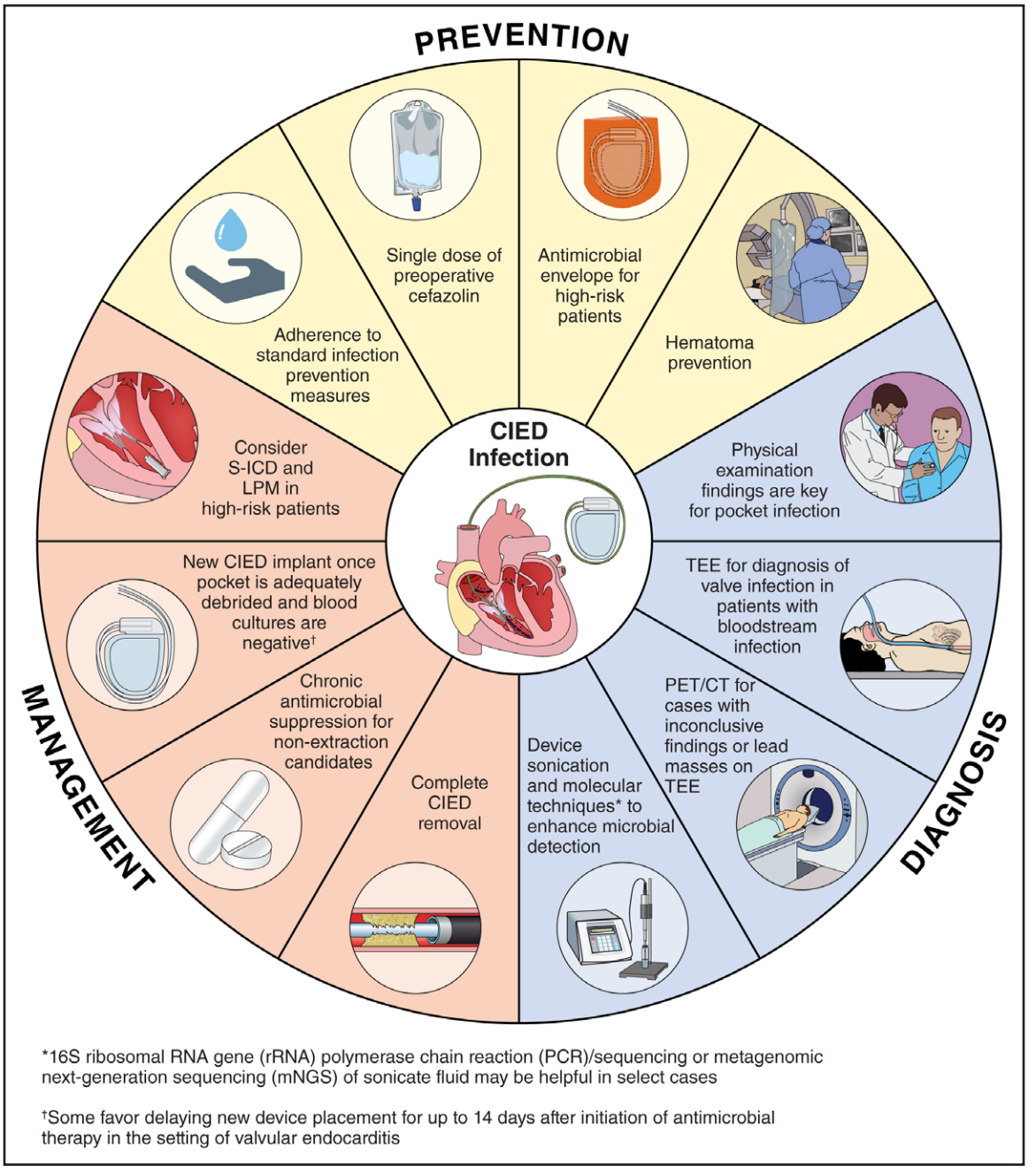

Figure 1. Central illustration.
CIED indicates cardiovascular implantable electronic device; LPM, leadless pacemaker; PET/CT, positron emission tomography/computerized tomography scanning; S-ICD, subcutaneous implantable cardioverter defibrillator; and TEE, transesophageal echocardiography.

include clinical practice recommendations. Nevertheless, suggested strategies have been outlined in the scientific statement with carefully drafted algorithms that will be useful to clinicians.

METHODS

A review process by the 11 WG members that included identification, acceptance, and approval by the AHA's manuscript oversight committee was initially conducted. After this, an initial orientation meeting with the WG Chair and Vice Chair and AHA administrative staff was held on October 19, 2022. The start-up call that included the WG members and administrative staff was held on October 26, 2022. An outline was reviewed that included key calendar dates for development and review of the scientific statement with ultimate publication within 12 months of the start date. An outline of the proposed scientific statement originally sent to the manuscript oversight committee included 3 major sections that were discussed by the WG and included (1) prevention; (2) diagnosis; and (3) management. Section leaders were selected with the expectation of hosting serial virtual meetings and a designation of writing commitments for each WG member with the goal of scientific statement completion within a 6-month period and subsequent transfer to the AHA for review.

An EndNote library of publications was provided by a Mayo Clinic librarian and was available for screening by WG members. Screened publications were limited to English language and were identified by a Medline and Embase search on October 28, 2022, with the search terms and format listed in the Supplemental Material (Supplemental Table 1). In the end, 743 publications were identified after duplicate publications were excluded. Each WG member had access to the list of publications that could be used as preparation for the development of this scientific statement. Citations advocated for by external reviewers of prepublication versions of the scientific statement were also included.

A penultimate draft of the scientific statement was provided to members of the International Society for Cardiovascular Infectious Diseases Council (http://iscvid.org/council-members/) for review and comment on April 30, 2023.

PREVENTION

Infection Prevention and Control Practice

Infection prevention measures taken pre-, peri-, and postoperatively have played a crucial role in decreasing rates of CIEDI. These measures have received limited attention in this scientific statement and are discussed in detail in the European Heart Rhythm Association international consensus document in 2019.[9]

Prevention of Hematoma

Do I Need to Stop or Change Anticoagulant Therapy for CIED Implantation/Revision?

Postprocedure pocket hematoma is associated with a significantly increased risk of infection requiring hospitalization within 1 year after the procedure.[10] Efforts to prevent hematoma formation, such as cautery of bleeding sites, irrigation of the pocket, and pressure dressings after skin closure, were described in the previous guideline.[2] Postoperative use of therapeutic heparin (both unfractionated and fractionated) can increase rates of hematoma formation after device placement.[11]

Many patients who require a CIED have underlying indications for anticoagulant therapy and are receiving oral agents such as warfarin and direct oral anticoagulants (DOACs). Since the 2010 AHA guidelines, 2 landmark clinical trials[12,13] have been completed that evaluated the role of continuing versus interrupted use of oral anticoagulants in patients at moderate to high risk of arterial thromboembolic events. The BRUISE CONTROL-1 study (Bridge or Continue Coumadin for Device Surgery Randomized Control Trial)[12] was a randomized control trial that included patients who were at high risk for thromboembolic events and were randomly assigned to either continued warfarin treatment or to bridging therapy with heparin, with the primary outcome focused on the development of clinically significant device-pocket hematoma. There was an 80% reduction in postoperative generator pocket hematoma in the continued warfarin group compared with that of the heparin-bridging group (3.5% versus 16.0%; $P<0.001$).[12] The WG believes an international normalized ratio range of 2 to 3.5 is acceptable for CIED implantation in patients taking warfarin.[14]

The BRUISE CONTROL-2 study[13] included patients with atrial fibrillation and a CHA_2DS_2-VASc score ≥2 who were randomly assigned to continued versus interrupted DOAC with the primary outcome of clinically significant pocket hematoma. The study was stopped for futility reasons after interim analysis in the first 662 patients showed that hematoma developed in 2.1% of patients in the continued DOAC and 2.1% in the interrupted group. Investigators concluded that either management strategy would be reasonable with low risk of hematoma formation.[13]

It is important to note that BRUISE CONTROL-1 did not examine the possibility of interrupted anticoagulation without bridging or antiplatelet therapy, whereas BRUISE CONTROL-2 did compare interrupted DOAC therapy versus not-interrupted therapy, but did not consider antiplatelet therapy. An analysis from WRAP-IT included 6800 study patients, of whom 86% were receiving anticoagulation (warfarin or DOAC) or antiplatelet therapy or both at the time of their CIED procedure.[15] Moreover, antiplatelet therapy increased the rate of hematoma formation independent of, but enhanced by concomitant

anticoagulation. Another analysis from WRAP-IT showed a 2.2% incidence of hematoma within 30 days and that hematomas of all sizes increased CIEDI risk by >11-fold.[16] Overall, hematoma prevention and anticoagulation and antiplatelet management may be the most important interventions in the prevention of CIEDI, exclusive of preoperative antibiotic administration and operative infection prevention and control measures.

Clinical Perspective

- Hematoma formation, regardless of size, is associated with a high risk of CIEDI; thus, prevention is critical.
- Continued or interrupted DOAC at the time of CIED implantation/revision are both acceptable because both are associated with a low risk of hematoma formation.
- In patients receiving warfarin, it is reasonable to perform CIED implantation with a therapeutic international normalized ratio between 2 and 3.5.

Procedural Antibiotic Prophylaxis

Is an Incremental Antibiotic Prophylaxis Approach Superior to Conventional Preoperative Antibiotic Prophylaxis With a First-Generation Cephalosporin?

The use of preprocedural antibiotics, most commonly a first-generation cephalosporin (eg, cefazolin) is standard practice and is supported by a large randomized clinical trial[17] and a meta-analysis of 7 clinical trials that included >2000 patients.[18] An additional dose of intraprocedural antibiotics may be considered if the duration from the time of antibiotic prophylaxis administration plus procedure time is >240 minutes.

Most device infections are due to gram-positive bacteria (Figure 2).[1,2] In a single-center analysis of the microbiology of CIEDI, for example, >70% of cases were due to staphylococci,[19] which reflects the microbiology of more contemporary studies.[9] Other gram-positive pathogens identified in this and other series include enterococci, streptococci, and *Cutibacterium* species. Many of these organisms are resistant to cefazolin, most notably methicillin-resistant *Staphylococcus aureus*, methicillin-resistant coagulase-negative staphylococci, and enterococci. Thus, the addition of vancomycin to β-lactam agents as routine preoperative prophylaxis has been considered. This regimen was examined in a large, cluster randomized crossover trial (the PADIT trial[3]) comparing conventional preoperative cefazolin with an incremental strategy of preoperative cefazolin plus vancomycin, intraprocedural bacitracin pocket wash, and 2-day postprocedural cephalexin. Among 19603 patients (12842 of whom were at high risk for infection), outcomes trended in favor of the incremental strategy; however, there was no statistically significant difference in hospitalization for device infection at 1 year in the high-risk group or any of the subgroups.

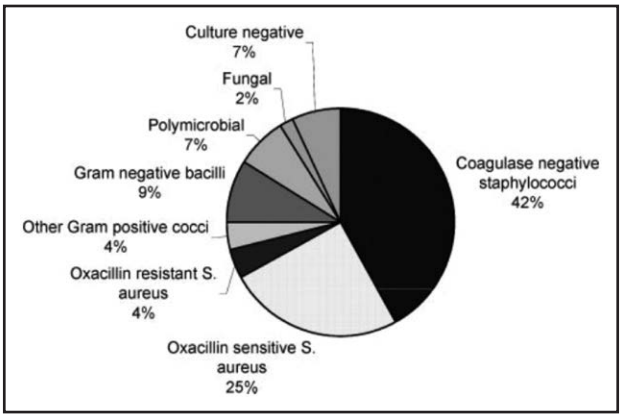

Figure 2. Microbiology of cardiovascular implantable electronic device infections.
Reprinted with permission from Sohail et al.[19] Copyright 2007, by the American College of Cardiology Foundation. Published by Elsevier.

Is Preoperative Prophylaxis With Vancomycin as Effective as First-Generation Cephalosporins in Preventing CIEDI?

Preprocedural vancomycin has not been shown to improve infectious outcomes compared with that with cefazolin[3,20,21]; and decisions regarding the use of vancomycin are based on its potential to promote antimicrobial resistance and actually increase the rate of methicillin-susceptible *S aureus* infections.[20,22]

Are There Other Procedural Strategies to Prevent CIEDI?

Regarding an intraoperative pocket wash, observational studies have demonstrated similar infection-related outcomes with antibiotic solutions compared with that of normal saline.[23,24] The use of postoperative oral antibiotics has not been associated with improved infection outcomes in observational studies[25,26] and the PADIT trial.[3]

From the WRAP-IT trial, 2803 control (no antibiotic envelope) patients who received standard preoperative antibiotics, both antibiotic pocket wash and chlorhexidine skin preparation, were associated with decreased risk of infection. In contrast, complete capsulectomy was associated with increased infection risk due to increased hematoma formation and infection.[27]

Clinical Perspective

- The use of preprocedural cefazolin is a data-supported standard practice.
- Vancomycin is an alternative in specific situations such as when the patient has a penicillin or β-lactam allergy, a history of methicillin-resistant *S aureus* infection, or a center has an unusually high rate of methicillin-resistant *S aureus* or methicillin-resistant coagulase-negative staphylococci infections on the basis of historical data. It is important to administer vancomycin 120 minutes before incision and weight-based dose of 20 mg/kg. Consider pharmacy guidance in patients with renal failure or obesity.

- The routine use of postoperative antibiotics is not supported by published data.
- Pocket irrigation with saline is reasonable for patients undergoing CIED implantation or generator replacement.
- Avoidance of capsulectomy to reduce hematoma formation and infection risk is advised.

Antibiotic-Eluting Envelope for CIEDI Prevention

Which Patients Are More Likely to Benefit From Antibiotic-Eluting Envelope Placement?

Pocket infection is responsible for about two-thirds of CIEDI, so strategies to prevent pocket infection are warranted. Incremental to other preparation and surgical techniques, antimicrobial envelopes deliver sustained-release antibiotics targeting the pocket inoculum that is inevitable. The device generator is inserted into an antimicrobial impregnated envelope and implanted in the device pocket. TYRX (by Medtronic Inc) is an absorbable envelope coated with minocycline and rifampin, eluting antibiotics in pocket tissue >7 days before the envelope is resorbed over the next 8 to 12 weeks.[28,29] In a multicenter randomized clinical trial that enrolled 6983 patients undergoing CIED revision, replacement, or upgrade, or de novo implantation of cardiac resynchronization therapy devices, major CIED-related infections occurred in 32 patients in the envelope group and 51 patients in the control group, offering a 40% relative risk reduction during 12 months follow-up.[4] In a subgroup analysis, envelope use resulted in a 76% reduction in staphylococcal pocket infections (P=0.010).[30] Tarakji et al[16] evaluated the association between antibiotic envelope use, hematoma, and CIEDI in patients enrolled in the WRAP-IT trial and found that the risk of CIEDI was reduced by 82% in patients who received an antibiotic envelope who developed hematoma compared with the control group without an antibiotic envelope. Because patients with lower body mass index have increased risk of hematoma, the use of an antibiotic envelope is reasonable.[15]

In a narrative review of 5 different investigations, use of an antibacterial envelope was associated with cost-effectiveness ratios below US and European benchmarks in selected patients at increased risk of infection.[31,32] These were nicely outlined in a review published in 2022.[33] On the basis of the willingness to pay threshold for each country, cost-effectiveness was associated with PADIT risk score ≥6 for all devices and history of immunosuppressive therapy in the 3 European countries (England, Germany, and Italy). There was variability among these countries on the basis of type of device and variables including ≥2 CIED procedures, previous CIEDI, replacement device, or generator replacement with lead modification. The type of device covered in all 3 countries varied, depending on the associated risk factor. For the US study, previous CIEDI was associated with cost saving, whereas cardiac resynchronization therapy with a defibrillator de novo implant was more costly than incremental cost-effectiveness ratio per quality-adjusted life-year.

Clinical Perspective

- Risk factors associated with CIEDI are well-defined and evaluation by a risk score may be useful in defining high risk (see Management section for details regarding risk score).
- Use of the antimicrobial envelope may be considered in patients at high risk of CIEDI, including patients at high risk of perioperative hematoma formation.

DIAGNOSIS

What Are the Challenges of Establishing a Diagnosis of CIEDI?

The diagnosis of CIEDI in patients with inflammatory findings at the pocket site is usually straightforward and is the most common presentation. However, establishing a diagnosis can be challenging in patients who present with positive blood cultures without generator pocket findings. At present, the European Heart Rhythm Association 2019 guidelines[9] have included echocardiography (transthoracic echocardiography and transesophageal echocardiography [TEE]) in defining CIEDI. This seems reasonable for detection of valve vegetations, which can occur in right-sided, left-sided, or bilateral IE. There are, however, key limitations in the ability of echocardiography in differentiating infected lead-related vegetations from noninfected clots or other masses. This misclassification of lead echodensities can affect the specificity of CIEDI diagnosis and potentially result in a false positive diagnosis of CIEDI on the basis of diagnostic criteria with resultant removal of a noninfected device. In addition, lead infection can be present without visualization of lead masses.

Duke criteria for IE diagnosis were first described in 1994[34] and originally developed for epidemiological and clinical trial purposes. They were subsequently modified in 2000[35] and have been adapted for use in defining CIEDI in individual patient management. The 2023 Duke-International Society for Cardiovascular Infectious Diseases criteria for IE are the most recent modification and include a more detailed evaluation of CIED-IE diagnosis.[7] However, these have not been specifically validated for the diagnosis of CIEDI. Therefore, the current WG developed clinical definitions of CIEDI with frontline clinicians in mind. We advocate for a comprehensive assessment of clinical, microbiological, and imaging findings in patients with suspected CIEDI with evaluation at medical centers with specialty expertise (Table).

Table. American Heart Association Clinical Definitions of Cardiovascular Implantable Electronic Device Infection

	Pocket infection	Lead or valvular infection
Definite	Preextraction Device erosion through skin; purulent drainage from pocket; fluctuance; sinus tract; with or without positive blood cultures OR [^{18}F]FDG PET/CT* with abnormal activity at pocket/generator site Postextraction Intraoperative findings consistent with infection, including purulence within the generator pocket site or inflammation OR Positive device, tissue, sonicate fluid cultures, positive broad range PCR/sequencing, or metagenomic next-generation sequencing with intraoperative findings consistent with infection	Preextraction Two or more positive blood cultures for *Staphylococcus aureus* or the same species of coagulase-negative staphylococci with no alternative source AND TEE findings consistent with echodensity on the device lead† or vegetation(s) on the heart valve OR [^{18}F]FDG PET/CT with abnormal heterogeneous activity along leads, or native or prosthetic heart valves Postextraction Positive device, tissue, sonicate fluid culture, broad range PCR/sequencing or metagenomic next-generation sequencing with the same organism isolated from blood cultures
Possible	Pocket erythema, induration, or tenderness within 3 mo of implantation, with no alternative explanation‡	Persistent (>72 h) bacteremia due to nonstaphylococcal organisms§ despite adequate pathogen-directed therapy, with no alternative source, ±TEE findings consistent with echodensity on the device lead OR embolic phenomena (frequently septic pulmonary emboli) Presence of SIRS criteria,‖ negative blood cultures, no alternative source of infection and [^{18}F]FDG PET/CT with abnormal activity along leads, or heart valves
Rejected	Firm alternative explanation for local findings that may include superficial cellulitis at the surgical site without device involvement, retained suture, contact dermatitis, or allergy to device components	Firm alternative source of bloodstream infection with resolution of syndrome after pathogen-directed treatment course TEE alone demonstrating a lead echodensity in the absence of SIRS criterial or positive blood cultures with alternative source of infection that responds to targeted antimicrobial therapy and source control.

These definitions are provided to support clinicians in their practice but are not intended as a substitute for clinical judgment. [^{18}F]FDG PET/CT indicates fluorine-18-fludeoxyglucose positron emission tomography/computerized tomography scanning; PCR, polymerase chain reaction; SIRS, systemic inflammatory response syndrome; and TEE, transesophageal echocardiography.

*Not required to establish a diagnosis.

†A negative TEE for lead echodensities does not rule out cardiovascular implantable electronic device lead infection.

‡Alternative explanations may include superficial cellulitis at the surgical site without device involvement, retained suture, contact dermatitis, or allergy to device components.

§Includes mainly nonstaphylococcal gram-positive organisms, *Pseudomonas aeruginosa*, *Serratia marcescens*, and *Candida* species.

‖SIRS criteria defined ≥ of the following: temperature ≥38.3°C or ≤36°C, pulse rate >90/min, respirations >20/min, and peripheral white blood cell count >12 000/μL or <4000/μL or >10% immature forms.

What Is the AHA Consensus Clinical Definition of a Definite CIEDI?

Physical examination findings involving the generator pocket, such as fluctuance, purulent drainage, device erosion through skin, or sinus tract formation, are considered definite criteria for pocket infection (Table). However, fluctuance alone could be due to a hematoma in the setting of recent CIED placement. Because hematoma is a well-recognized risk factor associated with CIEDI, a reevaluation by the multispecialty team is reasonable. Abnormal uptake at the pocket site can be seen on [^{18}F]FDG PET/CT but is not necessary to support a definite pocket infection when pocket site findings are present. Note that blood cultures would be collected in patients with local pocket site findings because a portion of them will have concomitant bloodstream infection and will require additional investigation (Figure 3).

In patients with fever or other systemic inflammatory response syndrome criteria who present without local findings at the pocket site, and in whom other alternative foci of infection have been ruled out, obtain at least 2 sets of blood cultures as soon as possible, ideally before the initiation of antibiotic therapy. The organism isolated from blood cultures determines the likelihood of CIEDI and coagulase-negative staphylococci and *S aureus* are the most common organisms identified in endovascular CIEDI cases. The isolation of either of these organisms from blood is consequently considered a criterion for definite infection (Table). Because coagulase-negative staphylococci are common blood culture contaminants, at least 2 sets of blood cultures drawn from different peripheral venous sites with the same species of coagulase-negative staphylococcus would be considered positive. When suspecting CIEDI, TEE findings need to be interpreted in the clinical and microbiological context and never as a standalone test. Although TEE is central in the diagnosis of valvular IE, which can complicate CIEDI, diagnostic specificity is a key limitation in establishing lead-related infection. Nevertheless, the presence of lead echodensities on TEE in the setting of staphylococcal bloodstream infection is highly suggestive of CIED lead infection. In the setting of nonstaphylococcal bacteremia, [^{18}F]FDG PET/CT uptake along leads may provide support for the diagnosis of CIED lead infection if the diagnosis is unclear.

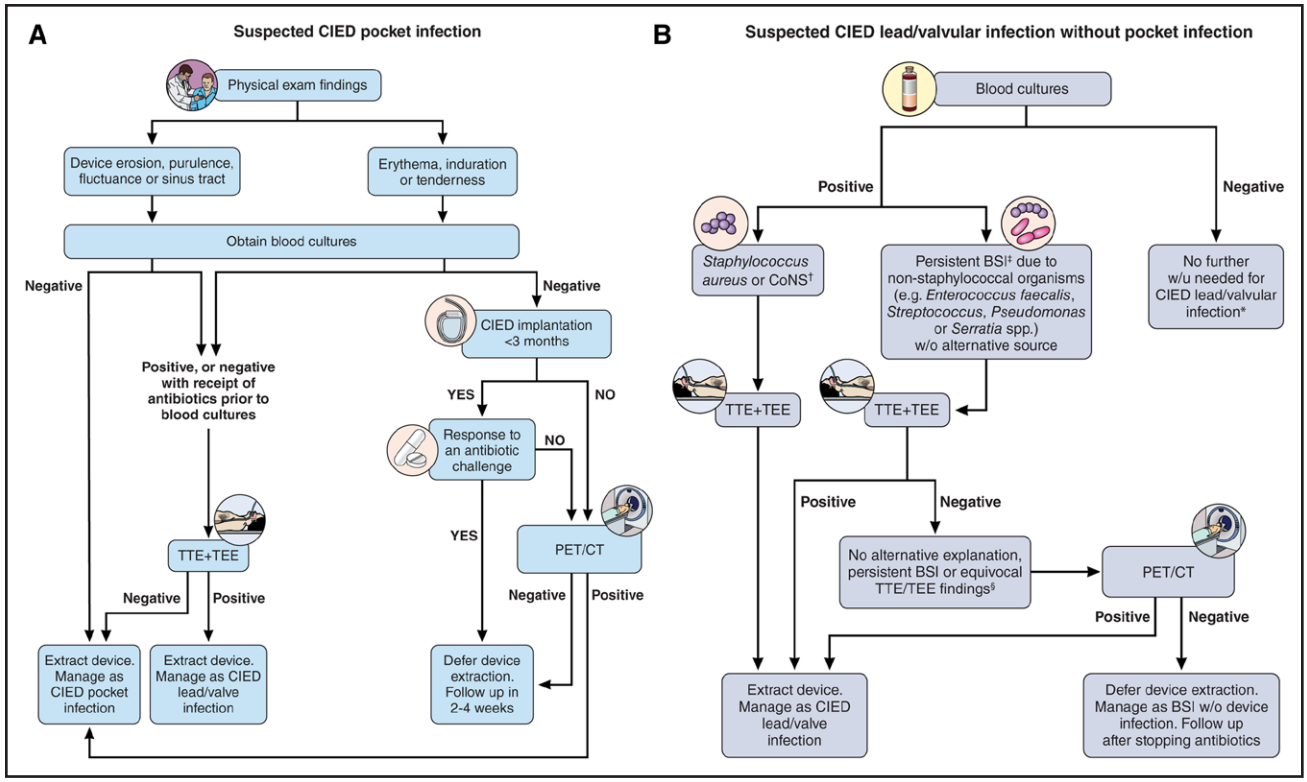

Figure 3. Diagnosis and management algorithms for suspected CIED pocket infection (A) and suspected CIED lead/valvular infection without pocket infection (B).

BSI indicates bloodstream infection; CIED, cardiovascular implantable electronic device; CoNS, coagulase-negative staphylococci; PET/CT, positron emission tomography/computerized tomography scanning; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; w/o, without; and w/up, work up.

What Is the AHA Consensus Clinical Definition of a Possible CIEDI?

In patients who present with superficial inflammatory signs at the pocket site, including erythema, tenderness, or induration, particularly if developed shortly after device implantation, it can be challenging to distinguish between device infection and superficial surgical site infection. As a result, these physical examination findings are categorized as possible pocket infections (Table). Local pocket superficial changes that fail to respond to or progress despite an antibiotic challenge (3–5 days) are likely representative of device infection.

Patients with CIED and persistent bloodstream infection, defined as positive blood cultures for >72 hours despite appropriate pathogen-directed antimicrobial therapy, with no alternative explanation, will need further evaluation for CIEDI regardless of the type of microorganism isolated from blood cultures. The diagnosis may be further supported by lead echodensities on TEE and septic emboli (frequently pulmonary emboli). In patients who have fever and other systemic inflammatory response syndrome criteria but have negative blood cultures and no defined source of infection, abnormal activity along leads or heart valves on [^{18}F]FDG PET/CT suggests CIED as the source of infection.

Clinical Perspective

- Physical examination changes at the generator pocket, such as fluctuance, purulent drainage, device erosion through skin, or sinus tract formation, are considered definite pocket infection.
- Patients with persistent *S aureus* or coagulase-negative staphylococcal bloodstream infection are at high risk of CIEDI and therefore should undergo timely device removal and antimicrobial therapy.
- Persistent bloodstream infection despite appropriate antimicrobial therapy due to nonstaphylococcal organisms raises concern for CIEDI, and treatment for such with complete device removal and continued antimicrobial therapy is reasonable if no alternative source of infection is established.

Imaging Modalities in the Diagnosis of CIEDI

Several investigators have questioned the role of TEE in the diagnosis of CIED lead infection because it cannot reliably distinguish between infectious and noninfectious

lead-related echodensities. As a result, episodes of bloodstream infection in patients with noninfectious lead echodensities could be mistakenly attributed to device infection, prompting unnecessary device removal. This has prompted interest in other emerging imaging modalities that incorporate metrics of inflammation, in particular, [^{18}F]FDG PET/CT[6,36] and white blood cell single-photon emission computed tomography/computed tomography.[37] These nuclear imaging studies have been proposed as adjunctive tests to increase the diagnostic accuracy of suspected CIEDI, in particular, in settings where other imaging modalities have failed to provide a definitive diagnosis. However, the associated financial cost, and local access to these screening tools, as well, and staff with expertise to interpret findings have been major limitations to adopting their widespread use. Discussion with your local nuclear medicine experts will be needed to ensure optimal test results using [^{18}F]FDG PET/CT, which may include carbohydrate restriction or sarcoid diet and other interventions. It is also important to consider that [^{18}F]FDG PET/CT and white blood cell single-photon emission computed tomography/computed tomography may both have reduced sensitivity in patients with low-grade pocket infection, lead infection, and in those who have received antibiotic therapy before imaging. Moreover, published data on the use of white blood cell single-photon emission computed tomography/computed tomography in the diagnosis of CIEDI have been markedly limited in comparison with that of [^{18}F]FDG PET/CT. Also, we are not aware of prospective comparator trials evaluating the usefulness of both imaging modalities. Availability may dictate the use of the modality chosen. Throughout this scientific statement, therefore, we have cited [^{18}F]FDG PET/CT as the preferred imaging modality.

The current WG secured consensus as it pertains to the use of imaging modalities in the diagnosis of CIEDI (Figure 3), with a discussion of strategies to address common conundrums that arise in CIEDI diagnosis in the discussion below. In addition, we have included examples of difficult clinical cases of suspected or proven CIEDI (Supplemental Table 2).

Suspected CIED Generator Pocket Infection

Is TEE Indicated in all Patients With CIED Pocket Infection?

TEE is important in patients with concomitant positive blood cultures or those who received antibiotic therapy before blood culture collection. In contrast, in patients with negative blood cultures and no recent antibiotic exposure, TEE is unlikely to provide additional information or to affect management decisions and is not indicated. However, TEE may be needed to define the procedural removal strategy of the device. Furthermore, TEE can also help determine the presence or absence of right-to-left shunts through the intra-atrial septum, assess the tricuspid valve status, and detect the presence or absence of pericardial effusion.

How Would PET/CT Be Used in Cases of Possible Pocket Infection?

In patients with device implantation within 3 months before presentation with subtle inflammatory signs at the pocket site, a suggested approach includes an empiric oral antibiotic challenge, usually with an antistaphylococcal antibiotic for 5 to 10 days. Device removal can be deferred in patients with the complete resolution of symptoms at the completion of therapy. However, close follow-up is advised to monitor for infection relapse. One approach is to perform [^{18}F]FDG PET/CT as early as possible in patients in whom antibiotic challenge fails and in those with CIED implantation >3 months from the development of local pocket site findings.

Suspected CIED Lead or Valvular Infection Without Generator Pocket Infection

What Imaging Tests Can Help With a Diagnosis in Patients With Possible CIED Lead Infection?

In cases where blood cultures are negative without recent antibiotic exposure, a multidisciplinary team evaluation to determine the diagnostic approach and management is advised. In cases of bloodstream infection due to nonstaphylococcal organisms where TEE is equivocal or does not support a diagnosis of infection, and a high index of suspicion remains either due to persistently positive blood cultures or no alternative source, [^{18}F]FDG PET/CT can be used to further investigate device infection in patients who are hemodynamically stable on appropriate pathogen-directed therapy. The combination of TEE plus [^{18}F]FDG PET/CT is complementary, increasing the diagnostic yield of systemic (endovascular and intracardiac lead) infections.[36]

What Is the Suggested Approach for Centers With No Access to [^{18}F]FDG PET/CT?

In patients with possible CIEDI who are medically stable at community hospitals without access to [^{18}F]FDG PET/CT, we suggest early referral to centers with access. If this is not feasible, an evaluation by a multidisciplinary team of experts in the fields of infectious diseases, clinical microbiology, cardiology, cardiovascular surgery, electrophysiology, and radiology is desirable. Likewise, for patients with possible CIEDI who are hemodynamically unstable, decisions regarding removal of a device are to be made without further delay on the basis of available evidence.

Clinical Perspective

- TEE remains an important diagnostic tool for evaluating patients with valvular infection or suspected CIEDI.

Circulation. 2023;148:e00–e00. DOI: 10.1161/CIR.0000000000001187

- A limitation of TEE is that this imaging modality cannot reliably distinguish between infectious and noninfectious lead echodensities or exclude lead infection without an echodensity.
- Although TEE may be deferred in patients with CIED pocket infection and negative blood cultures without previous antibiotics, it remains a useful tool for surgical planning for patients with a high suspicion of CIEDI where conventional imaging techniques have failed to provide a definitive diagnosis. [^{18}F]FDG PET/CT is a reasonable option to consider.
- [^{18}F]FDG PET/CT has reduced sensitivity in patients with low-grade pocket infection, lead infection, and in those who have received antibiotic therapy before imaging. As such, these tests might be considered in conjunction with other diagnostic tests and clinical judgment to ensure an accurate diagnosis and appropriate treatment.
- In patients with possible CIEDI who are medically stable at community hospitals without access to [^{18}F]FDG PET/CT, we suggest early referral to centers with access to these imaging modalities. If this is not feasible, an evaluation by a multidisciplinary team of experts in the diagnosis and management of CIEDI is advised.

Clinical Laboratory Advances in Pathogen Detection

In accordance with the 2010 AHA scientific statement,[2] blood and device specimens are to be collected and routine microbiological studies performed. In addition, there have been several laboratory advances in the detection of pathogens in the diagnosis of CIEDI. To enhance device culture sensitivity, vortexing sonification of explanted devices has been used for more than a decade in cases of prosthetic joint infection, and the technique is widely available among clinical laboratories. The technique has also been applied to other types of devices, including CIED with semiquantitative culture of sonicate fluid, which has increased the sensitivity of culture results compared with that of swab or tissue cultures.[38]

Culture methods may not be adequate in some cases of CIEDI, most often due to recent antimicrobial exposure. At present, many clinical and reference laboratories have adopted molecular techniques to increase pathogen detection in culture-negative cases of CIEDI. One approach includes 16S rRNA gene polymerase chain reaction/sequencing of sonicate fluid. In one recent series,[39] the sensitivity of polymerase chain reaction/sequencing was higher (64%) in sonicate fluid than that (57.5%) in sonicate fluid culture alone. In addition, polymerase chain reaction/sequencing detected a potential pathogen in 28 (23.8%) of 118 sonicate culture-negative cases.

A more recent investigation evaluated a different molecular technique, metagenomic next-generation sequencing (mNGS) in 110 patients with CIEDI.[40] Overall, the estimated sensitivity of mNGS in pathogen detection in sonicate fluid from extracted generators was 89%, whereas, for systemic infections, the sensitivity of mNGS for sonicate fluid from lead tips was only 48%.[40] mNGS is clearly of interest in defining pathogens in culture-negative CIEDI cases, and additional investigations are needed to better define its role.

Clinical Perspective

- A vortexing sonication technique of extracted CIED can improve the recovery of pathogens but is not available in all clinical settings.
- Due to limited availability in clinical laboratories, cost, and delayed culture results, selective use of molecular techniques may be considered in challenging cases; however, the results require careful interpretation within the clinical context.

Role of Inflammatory Markers in the Diagnosis of CIEDI

Inflammatory biomarkers have received limited attention in the diagnosis of CIEDI. As with many other syndromes of infection, routinely available markers, including peripheral leukocyte count and erythrocyte sedimentation rate, are not clinically reliable in the diagnosis of CIEDI and can be negative despite the presence of local pocket infection.[41] Other markers have undergone limited evaluation. There are data regarding use of procalcitonin levels in the diagnosis of CIEDI that are preliminary but suggest that this biomarker may be useful in diagnosis and could be used to differentiate local (pocket site) versus systemic infection.[42,43]

Clinical Perspective

- The diagnostic accuracy of procalcitonin in CIEDI deserves further investigation. Use of procalcitonin may be considered in conjunction with other clinical, laboratory, and imaging data.

MANAGEMENT

In accordance with the 2010 AHA guidelines,[2] definite CIEDI requires complete device removal, given the high rate of relapse with device retention (Figure 3). In addition, complete device removal has been advocated in all patients with valvular IE without definite device and lead involvement.[2]

Although there are no randomized controlled trials to determine the optimal timing of complete device removal, there are supportive survival data for early CIED extraction.[44,45] In the study by Le et al,[46] immediate CIEDI removal within 7 days of diagnosis compared with a delay in removal was associated with a 3-fold

decrease in 1-year mortality (hazard ratio, 0.35 [95% CI, 0.16–0.75]).

Empiric antibiotic therapy is only for use in a superficial incisional site infection, including a stitch abscess where device infection is not present. The device can be retained, and the superficial infection treated with a course of oral antimicrobial therapy.

The prevailing dogma is to avoid percutaneous pocket site aspiration to determine whether a pocket site infection is present in a patient with indeterminate pocket site changes. The concern is whether introduction of infection could occur with needle insertion for aspiration. Perhaps PET/CT could be helpful in differentiating pocket site infection in cases when device implantation was remote (>3 months earlier).

There are no clinical trials to direct the selection of an optimal antimicrobial treatment course in patients with CIEDI. For pocket site erosion without purulence, a 7-day duration after extraction is reasonable. For pocket site infection with purulence, a 10-day duration after extraction is reasonable. A longer duration of antimicrobial therapy is suggested in patients with bloodstream infection (Figure 3); patients with valvular IE may need up to 4 to 6 weeks of parenteral treatment, depending on the causative pathogen and whether there is native or prosthetic valve IE.

A recent randomized multicenter trial (POET [Partial Oral Treatment of Endocarditis]) examining the efficacy and safety of partial oral versus intravenous antibiotic therapy in patients with left-sided IE, found that step-down oral therapy was noninferior to continued intravenous antibiotic treatment.[47] Of note, in this study, 35 patients had a CIED at the time of IE diagnosis, of whom 14 were deemed to have CIED-related IE and underwent device removal. Eight of these patients were randomly assigned to the partial oral treatment group and the remaining 6 received prolonged intravenous therapy. Larger studies in this specific population are needed, however, to draw definitive conclusions.

Clinical Perspective

- Clinical trial data are lacking regarding optimal choice and duration of antimicrobial therapy.
- Early device removal has been associated with improved outcomes.

Timing of Reimplantation

What Is the Optimal Timing of Reimplantation?

Timing of reimplantation requires consideration of multiple factors; data to guide practice, however, are sparse. Overall, the incidence of reinfection after device reimplantation is low.[48–50] In a recent systematic review and meta-analysis, the incidence rate of device reinfection for the pooled cohort was 0.45% per person per year.[48] In contrast, mortality rate associated with various device reimplantation strategies ranged from 3% to 11% in the included studies (with varying durations of follow-up).[48] Underlying comorbidities and selection bias, however, are likely to play a greater role in mortality outcomes than is the timing of reimplantation.

As is consistent with society consensus documents (European Heart Rhythm Association,[9] Heart Rhythm Society [HRS][51]), the generally accepted practice is to delay reimplantation until signs and symptoms of local and systemic infection have resolved. It is desirable to delay new device implantation until other intravascular lines and undrained sites of infection have undergone adequate source control.[9,51] Although the optimal timing of new device placement remains undefined, a period after CIED removal of at least 3 days of negative blood cultures (to 14 days in patients with valvular IE) seems reasonable. Discussion of this aspect of care with other aspects of management in device-dependent patients by a team with endocarditis expertise is needed.

The use of a wearable defibrillator (LifeVest) is a reasonable strategy when delayed reimplantation of an ICD is desired. This strategy is useful in patients without an absolute pacing indication. A pacing lead attached to an externalized pacemaker (temporary permanent) could be used in pacemaker-dependent patients after extraction of an infected CIED while awaiting infection control.[52,53]

Clinical Perspective

- Delay reimplantation until signs and symptoms of local and systemic infection have resolved.
- Weigh the potential risks of early reimplantation with device dependency, and LPM or subcutaneous alternative devices.
- A wearable defibrillator and temporary-permanent pacemaker are reasonable strategies for patients in whom permanent device reimplantation is delayed.
- Consider delaying reimplantation up to 14 days when there is evidence of valvular IE.

Implantation of a New Device

What Are the Indications for Implantation of Newer Devices (Leadless Pacemaker and Subcutaneous Implantable Cardioverter Defibrillators)?

After device extraction, the indication for a new device is reassessed by the cardiac electrophysiologist. Conventional pacemakers and ICDs are associated with a high risk of complications related to the subcutaneous pocket and transvenous leads.[54,55] If a new device is needed in a patient with a previous CIEDI, then, according to recommendations in the 2010 AHA scientific statement, the new device would be implanted on the contralateral side, iliac vein, or epicardial position (Class I, Level of Evidence: C).[2] For epicardial lead placement, it could be an option among patients who have tricuspid valve abnormalities and need dual-chamber pacing. In recent years, LPM[56–58] and S-ICDs[59,60] have emerged as potential solutions to these problems.

Circulation. 2023;148:e00–e00. DOI: 10.1161/CIR.0000000000001187

The LPM consists of a self-contained generator and electrode system implanted preferably in the interventricular septum of the right ventricle by an endovascular femoral venous approach without the need for leads or subcutaneous pocket. Complication rates of LPM are comparable or lower than that of transvenous pacemakers for single-chamber devices.[61,62] However, it is associated with a higher rate of cardiac perforation and pericardial effusion.[61] The LPM may be considered among patients with a single-chamber ventricular pacing indication with high risk of infection. In the Micra investigational device exemption study, the Micra postapproval registry, and the AVEIR Leadless II-Phase II study, no device-related infection was reported among >3000 patients implanted with a LPM.[57,58,62] A subanalysis from the Micra investigational device exemption study described 16 patients implanted with a Micra LPM who developed bacteremia or IE during follow-up with predominantly a gram-positive organism. No evidence of device infection was seen; thus, device removal was not performed. Moreover, there were no cases of infection relapse. One patient had the device removed during aortic valve replacement for IE.[63] In another analysis from the Micra PAR investigation, 105 patients with previous CIEDI had their transvenous CIED extracted and were implanted with a Micra LPM (37% implanted the same day as the extraction).[64] No recurrent infection was seen in these patients. Other groups have reported on their experience with lead extractions of infected CIEDs and simultaneous implantation of Micra (at times, as a bridge for implantation of a permanent device).[65] There is emerging evidence that LPM can reduce the risk of CIEDI due to multiple mechanisms, mostly related to the absence of a subcutaneous pocket and potential for complete device endothelialization and encapsulation.[66] Given these data, LPM could be preferred in patients at high risk of infection requiring VVI pacing. Also, LPM could be implanted sooner to serve as a bridge to permanent CIED placement without the need for a long wait time between CIED extraction and reimplantation, especially in patients who otherwise might require temporary pacing and a long hospitalization before reimplantation. Whether an LPM is at reduced risk of infection compared with that of a transvenous pacemaker is currently undefined.

The S-ICD is entirely subcutaneous, eliminating the need for transvenous lead placement. It, however, has no pacing capacity. It has been proven that the S-ICD is noninferior to transvenous implantable cardioverter defibrillators (ICDs), and that it can be an efficacious alternative to the traditional ICD.[59] In a subanalysis from the PRAETORIAN randomized controlled study (A Prospective, Randomized Comparison of Subcutaneous and Transvenous Implantable Cardioverter Defibrillator Therapy), the S-ICD had a lower rate of lead-related complications and systemic infections compared with the transvenous ICD.[60] Likewise, the ATLAS trial (Assessment of Treatment with Lisinopril and Survival) showed a lower rate of lead-related complications, including infections with the S-ICD compared with transvenous ICD.[67] Implantation of a S-ICD may be considered among patients with ICD indications with high risk of infection (ie, previous CIED infection or IE, hemodialysis-dependent kidney disease, immunocompromisation, and congenital heart disease[68]).

In the recent position statement by the HRS, European HRS, Latin America HRS, and Asia Pacific HRS, the use of LPM and S-ICD was recommended in patients with a previous infection or at high risk of infection (ie, hemodialysis).[69]

Clinical Perspective

- It is reasonable to use LPM and S-ICD in patients at high risk of infection.
- The use of LPM after extraction of infected CIEDs might shorten the delay to reimplantation in the setting of systemic infection.

Role of Percutaneous Mechanical Aspiration for Vegetation Removal

Patients with right-sided IE may develop large (>2 cm) lead or right-sided valve vegetations that predispose to pulmonary embolization before and at the time of device removal. In addition, despite appropriate antimicrobial therapy, CIEDI may be complicated by persistent bloodstream infection and cardiogenic or septic shock. In response, reports during the past decade suggest that a minimally invasive approach using a percutaneous mechanical aspiration device may be useful in enhancing response to antimicrobial therapy, patient stabilization, reduction of pulmonary embolization risk before and at the time of lead removal, and an opportunity to obtain tissue for microbiological evaluation if previous blood cultures have failed to reveal a pathogen.

To date, there has been one multinational investigation[70] of percutaneous mechanical aspiration done in patients with CIEDI who have the following: (1) large (≥20 mm) lead vegetations; (2) small vegetations and persistent foramen ovale; (3) persistent bacteremia and sepsis in patients who are not candidates for device removal; and (4) patients with recurrent septic pulmonary emboli who are not candidates for device removal. Procedure success was reported in 95 (94.0%) of 101 patients with a low (3%) complication rate. A recent meta-analysis[71] that included both patients with right-sided IE who inject drugs and patients with CIEDI reported similar findings. Clinical trial data are sorely needed to better establish the role of this procedure in improving patient outcomes.

Clinical Perspective

- Percutaneous mechanical aspiration has been done in select cases, but clinical trial data are needed to better define the role of this procedure.

Approach to Patients With Retention of an Infected CIED

What Is the Role of Chronic Oral Antibiotic Suppressive Therapy?

Although necessary to attain cure, removal of an infected CIED is not always feasible. Patients with major comorbidities, high extraction risk, or limited life expectancy may not be candidates for device removal. Only one contemporary retrospective study has examined the outcomes of patients managed with device retention and chronic oral antimicrobial suppression (CAS).[72] This study reported a high relapse rate and mortality at 1 year. However, in cases where the risk of harm from system removal outweighs the benefit, we support recommendations by the 2010 AHA guidelines[2] to consider CAS therapy.

Initial Course of Therapy

For cases of presumed CIED lead or valvular infection managed with device retention, an intravenous route of antimicrobials is preferred as the initial course of treatment. Durations of therapy for lead and valvular CIEDI are depicted in Figure 3 of the 2010 AHA document.[2] Given the growing evidence of the safety and efficacy of oral antimicrobial therapy for treatment of endovascular infections, transition to an oral agent with high bioavailability may be reasonable once clinical stability and blood culture clearance has been achieved. Of note, in the recent randomized clinical trial examining partial oral versus intravenous treatment of IE (POET trial),[47] all cases attributed to a CIED underwent complete device removal. It is, therefore, unclear whether stepdown oral therapy could be applicable in cases managed with device retention, even when clinically stable; and more data are needed to endorse this practice.

CAS Therapy

Once initial treatment is completed, patients are transitioned to life-long oral antibiotic therapy guided by either experts in infectious diseases or clinical microbiology. In cases of pocket infection without bloodstream infection or systemic symptoms, pathogen-directed CAS therapy with an oral agent is preferred. If worsening erythema or drainage develops while receiving oral treatment, reevaluation of the patient and management strategy is warranted.

What Is the Role of Regional Antibiotic Delivery in Patients Without Complete Device Removal?

Although there have been case reports and small case series where direct instillation of antimicrobial therapy into an infected pocket site for attempted cure, data published in 2023[73] suggest that this approach may be feasible as a treatment option in patients who are either not candidates for complete device removal or unwilling to undergo removal. Of note, patients with *S aureus* infections were excluded from this initial analysis.[73] The installation procedure through a 6F indwelling catheter for a median of 12 days, so-called continuous, in situ-targeted, ultra-high concentration of antibiotics was used in 80 patients who had pocket site infection with no evidence of systemic infection. After a multistaged procedure, vancomycin with an aminoglycoside solution was used for initial loading followed by continuous infusion with monitoring of serum levels of antibiotics. Overall, 68 (85%) of 80 remained infection-free over a median follow-up of 3 years (interquartile range, 1.0–6.8 years).

Clinical Perspective

- Continuous, in situ-targeted, ultrahigh concentration of antibiotics may be an alternative in patients with CIEDI due to non–*S aureus* in circumstances where the risk of complete device removal is unacceptably high or among patients who decline device removal. More investigation is clearly needed before continuous, in situ-targeted, ultrahigh concentration of antibiotics is considered a management option.

Approach to Patients With Incomplete CIED Removal

In patients with CIED lead or valvular infection with abandoned leads, [^{18}F]FDG PET/CT[36] may be useful to evaluate for residual infection and whether CAS therapy is warranted. Lead tip retention is a relatively common outcome of extraction of leads with long dwell times. There are no data on the residual risk of these small distal fragments as a nidus for recurrent infection. The optimal timing between device removal and postoperative imaging is unknown; however, a delay of 4 to 6 weeks seems reasonable to decrease the likelihood of uptake due to postremoval inflammation. If access to [^{18}F]FDG PET/CT is not available, then it is reasonable to consider CAS therapy in patients who meet the clinical definition of a definite case (Table).

Clinical Perspective

- After completion of initial antibiotic therapy, CAS therapy may be considered in patients with CIEDI who are not candidates for complete device removal.
- Patients receiving CAS need early follow-up to evaluate for infection relapse and adverse drug events.
- In patients with incomplete device removal, [^{18}F]FDG PET/CT may be useful to evaluate for residual infection to determine whether CAS therapy is warranted.

Evidence Gaps and Future Considerations

Major advances in our understanding of CIEDI and its prevention, diagnosis, and management have occurred since publication of the 2010 scientific statement. Despite these achievements, there is much to be done to reduce the occurrence and clinical severity of this life-threatening syndrome. This includes defining an

optimal risk score to identify which patients would benefit from antimicrobial envelope use. There are currently no prospective trials to determine which score is most useful in defining the highest risk patients.

Additional investigation is needed to determine the role of 18-FDG PET/CT in the diagnosis of CIEDI and management of CAS in patients with no device removal. We also need more data on the use of molecular tools (polymerase chain reaction and mNGS) in cases of culture-negative CIEDI.

The optimal timing of complete device removal is another topic that requires more investigation. Moreover, the timing of new device implantation, for those who need it, warrants further study. Defining the subset of patients who would benefit from LPM or S-ICD implantation (if deemed an appropriate candidate), rather than a transvenous device deserves additional study. Considering the commonality of prosthetic valves and other cardiovascular devices in patients with CIEDI, more investigation is needed in defining diagnostic and management strategies.

Novel techniques including percutaneous mechanical aspiration and regional antibiotic delivery (continuous, in situ-targeted, ultrahigh concentration of antibiotics) for non–*S aureus* infections limited to the pocket site and are not candidates for complete device removal deserve further analysis as we consider interventions that may enhance patient outcomes. Additional pocket site antimicrobial delivery systems, such as impregnated sponges, are currently under investigation.

Disclosures

Writing Group Disclosures

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Larry M. Baddour	Mayo Clinic	None	None	None	None	None	None	None
Daniel C. DeSimone	Mayo Clinic	None	None	None	None	None	None	None
Jennifer N. Avari-Silva	Washington University/St. Louis Children's Hospital	Cardialen (DSMB, CEC)†	None	None	None	Sentiart†; Sentiar (immediate family members)†; Excera†; Excera (immediate family members)†	Sentiart†; Sentiar (immediate family members)†; Medtronic*; Abbott*; Biosense Webster*; Excera (unpaid)*; Excera (immediate family members (unpaid)*; iRhythm*	None
Vivian H. Chu	Duke University	None	None	None	None	None	None	None
Mikhael F. El-Chami	Emory University School of Medicine	Medtronic (research grant for an investigation-initiated study)*	None	None	None	None	Medtronic†; Boston Scientific*	None
Zerelda Esquer Garrigos	The University of Mississippi Medical Center	None	None	None	None	None	None	None
Eva Havers-Borgersen	Department of Cardiology, The Heart Centre, Rigshospitalet, Copenhagen University Hospital (Denmark)	None	None	None	None	None	None	None

(*Continued*)

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on September 1, 2023, and the American Heart Association Executive Committee on October 25, 2023. A copy of the document is available at https://professional.heart.org/statements by using either "Search for Guidelines & Statements" or the "Browse by Topic" area. To purchase additional reprints, call 215-356-2721 or email Meredith.Edelman@wolterskluwer.com

The American Heart Association requests that this document be cited as follows: Baddour LM, Esquer Garrigos Z, Sohail MR, Havers-Borgersen E, Krahn AD, Chu VH, Radke CS, Avari-Silva J, El-Chami MF, Miro JM, DeSimone DC; on behalf of the American Heart Association Council on Clinical Cardiology. Update on cardiovascular implantable electronic device infections and their prevention, diagnosis, and management: a scientific statement from the American Heart Association. *Circulation*. 2023;148:e•••–e•••. doi: 10.1161/CIR.0000000000001187

The expert peer review of AHA-commissioned documents (eg, scientific statements, clinical practice guidelines, systematic reviews) is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit https://professional.heart.org/statements. Select the "Guidelines & Statements" drop-down menu, then click "Publication Development."

Acknowledgments

The writing group thanks D.J. Gerberi, MLS, AHIP, for her expert assistance in performing the literature search and P. Lane for his contributions with professional illustration. Drs Chu and Miro were representatives of the International Society for Cardiovascular Infectious Diseases.

Writing Group Disclosures Continued

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Andrew D. Krahn	University of British Columbia (Canada)	None	None	None	None	None	None	None
Jose M. Miro	Hospital Clinic – IDIBAPS-CIBERINFEC, University of Barcelona (Spain)	None	80:20 research grant from IDIBAPS, Barcelona, Spain, during 2017–24, outside the submitted work†	None	None	None	None	None
Connie S. Radke	Omaha VA Medical Center	None	None	None	None	None	None	None
M. Rizwan Sohail	Baylor College of Medicine	None	None	None	None	None	Philips*; Angiodynamics*	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Mauro Biffi	Institute of Cardiology, Policlinico S.Orsola-Malpighi (Italy)	None	None	None	None	None	None	None
Kenneth A. Ellenbogen	Virginia Commonwealth University	None	None	Medtronic†	None	None	Medtronic†	None
Barry A. Love	Mount Sinai Medical Center	None	None	Medtronic*	None	None	Abbott*	None
Charles J. Love	Johns Hopkins Hospital	None	None	None	None	None	None	None
Bruce L. Wilkoff	Cleveland Clinic	None	None	Medtronic†; Boston Scientific*; Abbott*; Biotronik*; Philips†; Cook†; Xcardia*	None	None	Medtronic†; Philips†; Cook†; Xcardia*	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

REFERENCES

1. Hernández-Meneses M, Llopis J, Sandoval E, Ninot S, Almela M, Falces C, Pericàs JM, Vidal B, Perissinotti A, Marco F, et al; Hospital Clinic Infective Endocarditis Team Investigators. Forty-year trends in cardiac implantable electronic device infective endocarditis. *Open Forum Infect Dis*. 2022;9:ofac547. doi: 10.1093/ofid/ofac547
2. Baddour LM, Epstein AE, Erickson CC, Knight BP, Levison ME, Lockhart PB, Masoudi FA, Okum EJ, Wilson WR, Beerman LB, et al; on behalf of the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Nursing; Council on Clinical Cardiology; and the Interdisciplinary Council on Quality of Care and Outcomes Research. Update on cardiovascular implantable electronic device infections and their management: a scientific statement from the American Heart Association. *Circulation*. 2010;121:458–477. doi: 10.1161/CIRCULATIONAHA.109.192665
3. Krahn AD, Longtin Y, Philippon F, Birnie DH, Manlucu J, Angaran P, Rinne C, Coutu B, Low RA, Essebag V, et al. Prevention of arrhythmia device infection trial: the PADIT Trial. *J Am Coll Cardiol*. 2018;72:3098–3109. doi: 10.1016/j.jacc.2018.09.068
4. Tarakji KG, Mittal S, Kennergren C, Corey R, Poole JE, Schloss E, Gallastegui J, Pickett RA, Evonich R, Philippon F, et al; WRAP-IT Investigators. Antibacterial envelope to prevent cardiac implantable device infection. *N Engl J Med*. 2019;380:1895–1905. doi: 10.1056/NEJMoa1901111
5. George MP, Esquer Garrigos Z, Vijayvargiya P, Anavekar NS, Luis SA, Wilson WR, Baddour LM, Sohail MR. Discriminative ability and reliability of transesophageal echocardiography in characterizing cases of cardiac device lead vegetations versus noninfectious echodensities. *Clin Infect Dis*. 2021;72:1938–1943. doi: 10.1093/cid/ciaa472
6. Mahmood M, Kendi AT, Farid S, Ajmal S, Johnson GB, Baddour LM, Chareonthaitawee P, Friedman PA, Sohail MR. Role of ^{18}F-FDG PET/CT in the diagnosis of cardiovascular implantable electronic device infections: a meta-analysis. *J Nucl Cardiol*. 2019;26:958–970. doi: 10.1007/s12350-017-1063-0
7. Fowler VG, Durack DT, Selton-Suty C, Athan E, Bayer AS, Chamis AL, Dahl A, DiBernardo L, Durante-Mangoni E, Duval X, et al. The 2023 Duke-International Society for Cardiovascular Infectious Diseases criteria for infective endocarditis: updating the modified Duke criteria. *Clin Infect Dis*. 2023;77:518–526. doi: 10.1093/cid/ciad271
8. Malagù M, Donazzan L, Capanni A, Sirugo P, Rapezzi C, Bertini M. Risk scores for cardiac implantable electronic device infection: which one to believe in? *J Clin Med*. 2022;11:6556. doi: 10.3390/jcm11216556

9. Blomström-Lundqvist C, Traykov V, Erba PA, Burri H, Nielsen JC, Bongiorni MG, Poole J, Boriani G, Costa R, Deharo JC, 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;41:2012–2032. doi: 10.1093/eurheartj/ehaa010
10. Essebag V, Verma A, Healey JS, Krahn AD, Kalfon E, Coutu B, Ayala-Paredes F, Tang AS, Sapp J, Sturmer M, et al; BRUISE CONTROL Investigators. Clinically significant pocket hematoma increases long-term risk of device infection: BRUISE CONTROL INFECTION Study. *J Am Coll Cardiol*. 2016;67:1300–1308. doi: 10.1016/j.jacc.2016.01.009
11. Robinson M, Healey JS, Eikelboom J, Schulman S, Morillo CA, Nair GM, Baranchuk A, Ribas S, Evans G, Connolly SJ, et al. Postoperative low-molecular-weight heparin bridging is associated with an increase in wound hematoma following surgery for pacemakers and implantable defibrillators. *Pacing Clin Electrophysiol*. 2009;32:378–382. doi: 10.1111/j.1540-8159.2008.02247.x
12. Birnie DH, Healey JS, Wells GA, Verma A, Tang AS, Krahn AD, Simpson CS, Ayala-Paredes F, Coutu B, Leiria TL, et al; BRUISE CONTROL Investigators. Pacemaker or defibrillator surgery without interruption of anticoagulation. *N Engl J Med*. 2013;368:2084–2093. doi: 10.1056/NEJMoa1302946
13. Birnie DH, Healey JS, Wells GA, Ayala-Paredes F, Coutu B, Sumner GL, Becker G, Verma A, Philippon F, Kalfon E, et al. Continued vs. interrupted direct oral anticoagulants at the time of device surgery, in patients with moderate to high risk of arterial thrombo-embolic events (BRUISE CONTROL-2). *Eur Heart J*. 2018;39:3973–3979. doi: 10.1093/eurheartj/ehy413
14. AlTurki A, Proietti R, Birnie DH, Essebag V. Management of antithrombotic therapy during cardiac implantable device surgery. *J Arrhythm*. 2016;32:163–169. doi: 10.1016/j.joa.2015.12.003
15. Tarakji KG, Korantzopoulos P, Philippon F, Biffi M, Mittal S, Poole JE, Kennergren C, Lexcen DR, Lande JD, Hilleren G, et al. Risk factors for hematoma in patients undergoing cardiac device procedures: a WRAP-IT trial analysis. *Heart Rhythm O2*. 2022;3:466–473. doi: 10.1016/j.hroo.2022.05.012
16. Tarakji KG, Korantzopoulos P, Philippon F, Biffi M, Mittal S, Poole JE, Kennergren C, Lexcen DR, Lande JD, Seshadri S, et al. Infectious consequences of hematoma from cardiac implantable electronic device procedures and the role of the antibiotic envelope: a WRAP-IT trial analysis. *Heart Rhythm*. 2021;18:2080–2086. doi: 10.1016/j.hrthm.2021.07.011
17. de Oliveira JC, Martinelli M, Nishioka SA, Varejão T, Uipe D, Pedrosa AA, Costa R, D'Avila A, Danik SB. Efficacy of antibiotic prophylaxis before the implantation of pacemakers and cardioverter-defibrillators: results of a large, prospective, randomized, double-blinded, placebo-controlled trial. *Circ Arrhythm Electrophysiol*. 2009;2:29–34. doi: 10.1161/CIRCEP.108.795906
18. Da Costa A, Kirkorian G, Cucherat M, Delahaye F, Chevalier P, Cerisier A, Isaaz K, Touboul P. Antibiotic prophylaxis for permanent pacemaker implantation: a meta-analysis. *Circulation*. 1998;97:1796–1801. doi: 10.1161/01.cir.97.18.1796
19. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR, Steckelberg JM, Stoner S, Baddour LM. Management and outcome of permanent pacemaker and implantable cardioverter-defibrillator infections. *J Am Coll Cardiol*. 2007;49:1851–1859. doi: 10.1016/j.jacc.2007.01.072
20. Finkelstein R, Rabino G, Mashiah T, Bar-El Y, Adler Z, Kertzman V, Cohen O, Milo S. Vancomycin versus cefazolin prophylaxis for cardiac surgery in the setting of a high prevalence of methicillin-resistant staphylococcal infections. *J Thorac Cardiovasc Surg*. 2002;123:326–332. doi: 10.1067/mtc.2002.119698
21. Alzahrani T, Liappis AP, Baddour LM, Karasik PE. Preoperative antibiotics and cardiovascular implantable electronic device infection: a cohort study in veterans. *Pacing Clin Electrophysiol*. 2018;41:1513–1518. doi: 10.1111/pace.13499
22. Bull AL, Worth LJ, Richards MJ. Impact of vancomycin surgical antibiotic prophylaxis on the development of methicillin-sensitive *Staphylococcus aureus* surgical site infections: report from Australian Surveillance Data (VICNISS). *Ann Surg*. 2012;256:1089–1092. doi: 10.1097/SLA.0b013e31825fa398
23. Lakshmanadoss U, Nuanez B, Kutinsky I, Khalid R, Haines DE, Wong WS. Incidence of pocket infection postcardiac device implantation using antibiotic versus saline solution for pocket irrigation. *Pacing Clin Electrophysiol*. 2016;39:978–984. doi: 10.1111/pace.12920
24. Rodriguez D, Thurber CJ, Romero JE, Sauer WH, Kapur S, Tadros TM, Koplan BA. Device pocket antibiotic irrigation provides no CIED-pocket infection prophylaxis advantage compared to normal saline. *JACC Clin Electrophysiol*. 2022;8:1319–1320. doi: 10.1016/j.jacep.2022.05.018
25. Kabulski GM, Northup A, Wiggins BS. Postoperative antibiotic prophylaxis following cardiac implantable electronic device placement. *J Innov Card Rhythm Manag*. 2019;10:3777–3784. doi: 10.19102/icrm.2019.100804
26. Madadi S, Kafi M, Kheirkhah J, Azhari A, Kiarsi M, Mehryar A, Fazelifar A, Alizadehdiz A, Emkanjoo Z, Haghjoo M. Postoperative antibiotic prophylaxis in the prevention of cardiac implantable electronic device infection. *Pacing Clin Electrophysiol*. 2019;42:161–165. doi: 10.1111/pace.13592
27. Tarakji KG, Krahn AD, Poole JE, Mittal S, Kennergren C, Biffi M, Korantzopoulos P, Dallaglio PD, Lexcen DR, Lande JD, et al. Risk factors for CIED infection after secondary procedures: insights from the WRAP-IT trial. *JACC Clin Electrophysiol*. 2022;8:101–111. doi: 10.1016/j.jacep.2021.08.009
28. Henrikson CA, Sohail MR, Acosta H, Johnson EE, Rosenthal L, Pachulski R, Dan D, Paladino W, Khairallah FS, Gleed K, et al. Antibacterial envelope is associated with low infection rates after implantable cardioverter-defibrillator and cardiac resynchronization therapy device replacement: results of the Citadel and Centurion studies. *JACC Clin Electrophysiol*. 2017;3:1158–1167. doi: 10.1016/j.jacep.2017.02.016
29. Tarakji KG, Mittal S, Kennergren C, Corey R, Poole J, Stromberg K, Lexcen DR, Wilkoff BL. Worldwide randomized antibiotic envelope infection prevention trial (WRAP-IT). *Am Heart J*. 2016;180:12–21. doi: 10.1016/j.ahj.2016.06.010
30. Sohail MR, Corey GR, Wilkoff BL, Poole JE, Mittal S, Kennergren C, Greenspon AJ, Cheng A, Lande JD, Lexcen DR, et al. Clinical presentation, timing, and microbiology of CIED infections: an analysis of the WRAP-IT trial. *JACC Clin Electrophysiol*. 2021;7:50–61. doi: 10.1016/j.jacep.2020.07.021
31. Boriani G, Vitolo M, Wright DJ, Biffi M, Brown B, Tarakji KG, Wilkoff BL. Infections associated with cardiac electronic implantable devices: economic perspectives and impact of the TYRX™ antibacterial envelope. *Europace*. 2021;23:iv33–iv44. doi: 10.1093/europace/euab126
32. Birnie DH, Wang J, Alings M, Philippon F, Parkash R, Manlucu J, Angaran P, Rinne C, Coutu B, Low RA, et al. Risk factors for infections involving cardiac implanted electronic devices. *J Am Coll Cardiol*. 2019;74:2845–2854. doi: 10.1016/j.jacc.2019.09.060
33. Traykov V, Blomström-Lundqvist C. Antibiotic-eluting envelopes for the prevention of cardiac implantable electronic device infections: rationale, efficacy, and cost-effectiveness. *Front Cardiovasc Med*. 2022;9:855233. doi: 10.3389/fcvm.2022.855233
34. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings Duke Endocarditis Service. *Am J Med*. 1994;96:200–209. doi: 10.1016/0002-9343(94)90143-0
35. Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, Bashore T, Corey GR. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis*. 2000;30:633–638. doi: 10.1086/313753
36. Hernández-Meneses M, Perissinotti A, Páez-Martínez S, Llopis J, Dahl A, Sandoval E, Falces C, Ambrosioni J, Vidal B, Marco F, et al; Hospital Clínic of Barcelona Infective Endocarditis Team Investigators. Reappraisal of [18F] FDG-PET/CT for diagnosis and management of cardiac implantable electronic device infections. *Rev Esp Cardiol (Engl Ed)*. Published online April 6, 2023;S1885–5857(23)00101. doi: 10.1016/j.rec.2023.04.001
37. Erba PA, Sollini M, Conti U, Bandera F, Tascini C, De Tommasi SM, Zucchelli G, Doria R, Menichetti F, Bongiorni MG, et al. Radiolabeled WBC scintigraphy in the diagnostic workup of patients with suspected device-related infections. *JACC Cardiovasc Imaging*. 2013;6:1075–1086. doi: 10.1016/j.jcmg.2013.08.001
38. Nagpal A, Patel R, Greenwood-Quaintance KE, Baddour LM, Lynch DT, Lahr BD, Maleszewski JJ, Friedman PA, Hayes DL, Sohail MR. Usefulness of sonication of cardiovascular implantable electronic devices to enhance microbial detection. *Am J Cardiol*. 2015;115:912–917. doi: 10.1016/j.amjcard.2015.01.017
39. Esquer Garrigos Z, Sohail MR, Greenwood-Quaintance KE, Cunningham SA, Vijayvargiya P, Fida M, Friedman PA, Mandrekar J, DeSimone DC, Baddour LM, et al. Molecular approach to diagnosis of cardiovascular implantable electronic device infection. *Clin Infect Dis*. 2020;70:898–906. doi: 10.1093/cid/ciz266
40. Olsen T, Justesen US, Nielsen JC, Jørgensen OD, Sandgaard NCF, Ravn C, Gerdes C, Thøgersen AM, Gill S, Fuursted K, et al. Microbiological diagnosis in cardiac implantable electronic device infections detected by sonication and next-generation sequencing. *Heart Rhythm*. 2022;19:901–908. doi: 10.1016/j.hrthm.2022.01.039

41. Lennerz C, Vrazic H, Haller B, Braun S, Petzold T, Ott I, Lennerz A, Michel J, Blažek P, Deisenhofer I, et al. Biomarker-based diagnosis of pacemaker and implantable cardioverter defibrillator pocket infections: a prospective, multicentre, case-control evaluation. *PLoS One*. 2017;12:e0172384. doi: 10.1371/journal.pone.0172384
42. Ząbek A, Ulman M, Holcman K, Boczar K, Dębski M, Kostkiewicz M, Lelakowski J, Małecka B. Inflammatory markers in the diagnostic workup of pacemaker- and defibrillator-related infections in patients referred for transvenous lead extraction. *Kardiol Pol*. 2019;77:918–925. doi: 10.33963/KP.14934
43. Knoll K, O'Connor M, Chouchane A, Haller B, Schaarschmidt C, Bock M, Förschner L, Fröhlich R, Kottmaier M, Bourier F, et al. A prospective case-control validation of procalcitonin as a biomarker diagnosing pacemaker and implantable cardioverter-defibrillator pocket infection. *Kardiol Pol*. 2022;80:782–791. doi: 10.33963/KP.a2022.0124
44. Han HC, Wang J, Birnie DH, Alings M, Philippon F, Parkash R, Manlucu J, Angaran P, Rinne C, Coutu B, et al. Association of the timing and extent of cardiac implantable electronic device infections with mortality. *JAMA Cardiol*. 2023;8:484–491. doi: 10.1001/jamacardio.2023.0467
45. Lakkireddy DR, Segar DS, Sood A, Wu M, Rao A, Sohail MR, Pokorney SD, Blomström-Lundqvist C, Piccini JP, Granger CB. Early lead extraction for infected implanted cardiac electronic devices: JACC review topic of the week. *J Am Coll Cardiol*. 2023;81:1283–1295. doi: 10.1016/j.jacc.2023.01.038
46. Le KY, Sohail MR, Friedman PA, Uslan DZ, Cha SS, Hayes DL, Wilson WR, Steckelberg JM, Baddour LM; Mayo Cardiovascular Infections Study Group. Impact of timing of device removal on mortality in patients with cardiovascular implantable electronic device infections. *Heart Rhythm*. 2011;8:1678–1685. doi: 10.1016/j.hrthm.2011.05.015
47. Iversen K, Ihlemann N, Gill SU, Madsen T, Elming H, Jensen KT, Bruun NE, Høfsten DE, Fursted K, Christensen JJ, et al. Partial oral versus intravenous antibiotic treatment of endocarditis. *N Engl J Med*. 2019;380:415–424. doi: 10.1056/NEJMoa1808312
48. Chew D, Somayaji R, Conly J, Exner D, Rennert-May E. Timing of device reimplantation and reinfection rates following cardiac implantable electronic device infection: a systematic review and meta-analysis. *BMJ Open*. 2019;9:e029537. doi: 10.1136/bmjopen-2019-029537
49. Boyle TA, Uslan DZ, Prutkin JM, Greenspon AJ, Baddour LM, Danik SB, Tolosana JM, Le K, Miro JM, Peacock J, et al. Reimplantation and repeat infection after cardiac-implantable electronic device infections: experience from the MEDIC (Multicenter Electrophysiologic Device Infection Cohort) database. *Circ Arrhythm Electrophysiol*. 2017;10:e004822. doi: 10.1161/CIRCEP.116.004822
50. Arshad V, Baddour LM, Lahr BD, Khalil S, Tariq W, Talha KM, Cha YM, DeSimone DC, Sohail MR. Impact of delayed device re-implantation on outcomes of patients with cardiovascular implantable electronic device related infective endocarditis. *Pacing Clin Electrophysiol*. 2021;44:1303–1311. doi: 10.1111/pace.14297
51. Kusumoto FM, Schoenfeld MH, Wilkoff BL, Berul CI, Birgersdotter-Green UM, Carrillo R, Cha YM, Clancy J, Deharo JC, Ellenbogen KA, et al. 2017 HRS expert consensus statement on cardiovascular implantable electronic device lead management and extraction. *Heart Rhythm*. 2017;14:e503–e551. doi: 10.1016/j.hrthm.2017.09.001
52. Braun MU, Rauwolf T, Bock M, Kappert U, Boscheri A, Schnabel A, Strasser RH. Percutaneous lead implantation connected to an external device in stimulation-dependent patients with systemic infection: a prospective and controlled study. *Pacing Clin Electrophysiol*. 2006;29:875–879. doi: 10.1111/j.1540-8159.2006.00454.x
53. Kornberger A, Schmid E, Kalender G, Stock UA, Doernberger V, Khalil M, Lisy M. Bridge to recovery or permanent system implantation: an eight-year single-center experience in transvenous semipermanent pacing. *Pacing Clin Electrophysiol*. 2013;36:1096–1103. doi: 10.1111/pace.12175
54. Kirkfeldt RE, Johansen JB, Nohr EA, Jørgensen OD, Nielsen JC. Complications after cardiac implantable electronic device implantations: an analysis of a complete, nationwide cohort in Denmark. *Eur Heart J*. 2014;35:1186–1194. doi: 10.1093/eurheartj/eht511
55. Udo EO, Zuithoff NP, van Hemel NM, de Cock CC, Hendriks T, Doevendans PA, Moons KG. Incidence and predictors of short- and long-term complications in pacemaker therapy: the FOLLOWPACE study. *Heart Rhythm*. 2012;9:728–735. doi: 10.1016/j.hrthm.2011.12.014
56. El-Chami MF, Al-Samadi F, Clementy N, Garweg C, Martinez-Sande JL, Piccini JP, Iacopino S, Lloyd M, Viñolas Prat X, Jacobsen MD, et al. Updated performance of the Micra transcatheter pacemaker in the real-world setting: a comparison to the investigational study and a transvenous historical control. *Heart Rhythm*. 2018;15:1800–1807. doi: 10.1016/j.hrthm.2018.08.005
57. Reynolds D, Duray GZ, Omar R, Soejima K, Neuzil P, Zhang S, Narasimhan C, Steinwender C, Brugada J, Lloyd M, et al; Micra Transcatheter Pacing Study Group. A leadless intracardiac transcatheter pacing system. *N Engl J Med*. 2016;374:533–541. doi: 10.1056/NEJMoa1511643
58. Reddy VY, Exner DV, Doshi R, Tomassoni G, Bunch TJ, Estes NAM, Neužil P, Paulin FL, Garcia Guerrero JJ, Cantillon DJ; LEADLESS II Investigators. Primary results on safety and efficacy from the LEADLESS II-Phase 2 worldwide clinical trial. *JACC Clin Electrophysiol*. 2022;8:115–117. doi: 10.1016/j.jacep.2021.11.002
59. Knops RE, Olde Nordkamp LRA, Delnoy PHM, Boersma LVA, Kuschyk J, El-Chami MF, Bonnemeier H, Behr ER, Brouwer TF, Kääb S, et al. Subcutaneous or transvenous defibrillator therapy. *N Engl J Med*. 2020;383:526–536. doi: 10.1056/NEJMoa1915932
60. Knops RE, Pepplinkhuizen S, Delnoy P, Boersma LVA, Kuschyk J, El-Chami MF, Bonnemeier H, Behr ER, Brouwer TF, Kaab S, et al. Device-related complications in subcutaneous versus transvenous ICD: a secondary analysis of the PRAETORIAN trial. *Eur Heart J*. 2022;43:4872–4883. doi: 10.1093/eurheartj/ehac496
61. Piccini JP, El-Chami M, Wherry K, Crossley GH, Kowal RC, Stromberg K, Longacre C, Hinnenthal J, Bockstedt L. Contemporaneous comparison of outcomes among patients implanted with a leadless vs transvenous single-chamber ventricular pacemaker. *JAMA Cardiol*. 2021;6:1187–1195. doi: 10.1001/jamacardio.2021.2621
62. El-Chami MF, Bockstedt L, Longacre C, Higuera L, Stromberg K, Crossley G, Kowal RC, Piccini JP. Leadless vs transvenous single-chamber ventricular pacing in the Micra CED study: 2-year follow-up. *Eur Heart J*. 2022;43:1207–1215. doi: 10.1093/eurheartj/ehab767
63. El-Chami MF, Soejima K, Piccini JP, Reynolds D, Ritter P, Okabe T, Friedman PA, Cha YM, Stromberg K, Holbrook R, et al. Incidence and outcomes of systemic infections in patients with leadless pacemakers: data from the Micra IDE study. *Pacing Clin Electrophysiol*. 2019;42:1105–1110. doi: 10.1111/pace.13752
64. El-Chami MF, Johansen JB, Zaidi A, Faerestrand S, Reynolds D, Garcia-Seara J, Mansourati J, Pasquie JL, McElderry HT, Roberts PR, et al. Leadless pacemaker implant in patients with pre-existing infections: results from the Micra postapproval registry. *J Cardiovasc Electrophysiol*. 2019;30:569–574. doi: 10.1111/jce.13851
65. Chang D, Gabriels JK, Soo Kim B, Ismail H, Willner J, Beldner SJ, John RM, Epstein LM. Concomitant leadless pacemaker implantation and lead extraction during an active infection. *J Cardiovasc Electrophysiol*. 2020;31:860–867. doi: 10.1111/jce.14390
66. El-Chami MF, Bonner M, Holbrook R, Stromberg K, Mayotte J, Molan A, Sohail MR, Epstein LM. Leadless pacemakers reduce risk of device-related infection: review of the potential mechanisms. *Heart Rhythm*. 2020;17:1393–1397. doi: 10.1016/j.hrthm.2020.03.019
67. Healey JS, Krahn AD, Bashir J, Amit G, Philippon F, McIntyre WF, Tsang B, Joza J, Exner DV, Birnie DH, et al; ATLAS Investigators. Perioperative safety and early patient and device outcomes among subcutaneous versus transvenous implantable cardioverter defibrillator implantations: a randomized, multicenter trial. *Ann Intern Med*. 2022;175:1658–1665. doi: 10.7326/M22-1566
68. Havers-Borgersen E, Butt JH, Østergaard L, Petersen JK, Torp-Pedersen C, Køber L, Fosbøl EL. Long-term incidence of infective endocarditis among patients with congenital heart disease. *Am Heart J*. 2023;259:9–20. doi: 10.1016/j.ahj.2023.01.012
69. Boersma LV, El-Chami M, Steinwender C, Lambiase P, Murgatroyd F, Mela T, Theuns D, Khelae SK, Kalil C, Zabala F, et al. Practical considerations, indications, and future perspectives for leadless and extravascular cardiac implantable electronic devices: a position paper by EHRA/HRS/LAHRS/APHRS. *Europace*. 2022;24:1691–1708. doi: 10.1093/europace/euac066
70. Starck CT, Schaerf RHM, Breitenstein A, Najibi S, Conrad J, Berendt J, Esmailian F, Eulert-Grehn J, Dreizler T, Falk V. Transcatheter aspiration of large pacemaker and implantable cardioverter-defibrillator lead vegetations facilitating safe transvenous lead extraction. *Europace*. 2020;22:133–138. doi: 10.1093/europace/euz283
71. Mhanna M, Beran A, Al-Abdouh A, Jabri A, Sajdeya O, Al-Aaraj A, Alharbi A, Khuder SA, Eltahawy EA. AngioVac for vegetation debulking in right-sided infective endocarditis: a systematic review and meta-analysis. *Curr Probl Cardiol*. 2022;47:101353. doi: 10.1016/j.cpcardiol.2022.101353
72. Tan EM, DeSimone DC, Sohail MR, Baddour LM, Wilson WR, Steckelberg JM, Virk A. Outcomes in patients with cardiovascular implantable electronic device infection managed with chronic antibiotic suppression. *Clin Infect Dis*. 2017;64:1516–1521. doi: 10.1093/cid/cix181
73. Topaz M, Chorin E, Schwartz AL, Hochstadt A, Shotan A, Ashkenazi I, Kazatsker M, Carmel NN, Topaz G, Oron Y, et al. Regional antibiotic delivery for implanted cardiovascular electronic device infections. *J Am Coll Cardiol*. 2023;81:119–133. doi: 10.1016/j.jacc.2022.10.022