ESC European Society of Cardiology

Europace (2021) **23**, iv20–iv27
doi:10.1093/europace/euab016

SUPPLEMENT PAPER

Therapy and outcomes of cardiac implantable electronic devices infections

Tilman Perrin [1,2] **and Jean-Claude Deharo** [2]*

[1]Department of Cardiology, Solothurner Spitäler Bürgerspital, Solothurn, Switzerland; and [2]Department of Cardiology, Centre Hospitalier Universitaire La Timone, 264 Rue Saint-Pierre, F-13005 Marseille, France

Received 14 December 2020; editorial decision 3 January 2021; accepted after revision 13 January 2021

Abstract Cardiac implantable electronic device (CIED) infection causes significant morbidity and mortality without appropriate treatment. It can present as incisional infection, pocket infection, systemic CIED infection, or occult bacteraemia. Complete percutaneous CIED extraction (excepted in case of incisional infection) and appropriate antibiotic therapy are the two main pillars of therapy. Device reimplantation, if needed, should be delayed sufficiently to allow control of the infection. Here, we address the differences in prognosis according to the clinical scenario and the different treatment options.

Keywords Antibiotic therapy • Implantable electronic device infection • Lead endocarditis • Percutaneous lead extraction • Reimplantation

Introduction

Implantation of pacemakers (PM) and implantable cardioverter-defibrillators (ICD) is on the rise, due to widening of indications and ageing population.[1] Device-therapy is effective for the treatment of cardiac arrhythmias and improves prognosis and symptoms in selected patients,[2–4] but cardiac implantable electronic device (CIED) infection is a feared complication causing significant morbidity and mortality. Despite technological improvements and standardized protocols, the rate of CIED infections increases even out of proportion to the rate of new device implants.[5] In the recent report from the Danish device-cohort (1982–2018), the combined lifetime incidence of systemic endocarditis and pocket infection was reported to increase with the complexity of the devices from 1.19% for PM to 3.35% for CRT-D systems.[6]

Our review addresses the outcomes related (i) to the different clinical scenarios of CIED infection, (ii) to the extraction of infected leads, and (iii) to the available CIED reimplantation strategies in patients explanted because of device infection.

Clinical scenarios of cardiac implantable electronic device infection and their outcomes

Cardiac implantable electronic device infection occurs through contamination of leads and/or pulse generator during device procedures or by bloodstream infection at times of bacteraemia.[7] Four main clinical scenarios can be differentiated, with major consequences on therapy. *Figure 1* depicts our practical diagnosis and treatment approach for management of CIED infection.

Superficial incisional infection

A superficial incisional infection involves only the skin and the superficial subcutaneous tissue of the incision, but not the deep soft tissues (e.g. fascia, muscle, and/or pocket).[8] Per definition it is associated with a recent device procedure (device implantation, revision, or replacement). *Staphylococcus aureus* is the most frequently involved pathogen. Wound cultures are recommended before initiation of

* Corresponding author . Tel: +33 4 91 38 65 75; fax: +33 4 91 38 64 70. *E-mail address*: JeanClaude.DEHARO@ap-hm.fr

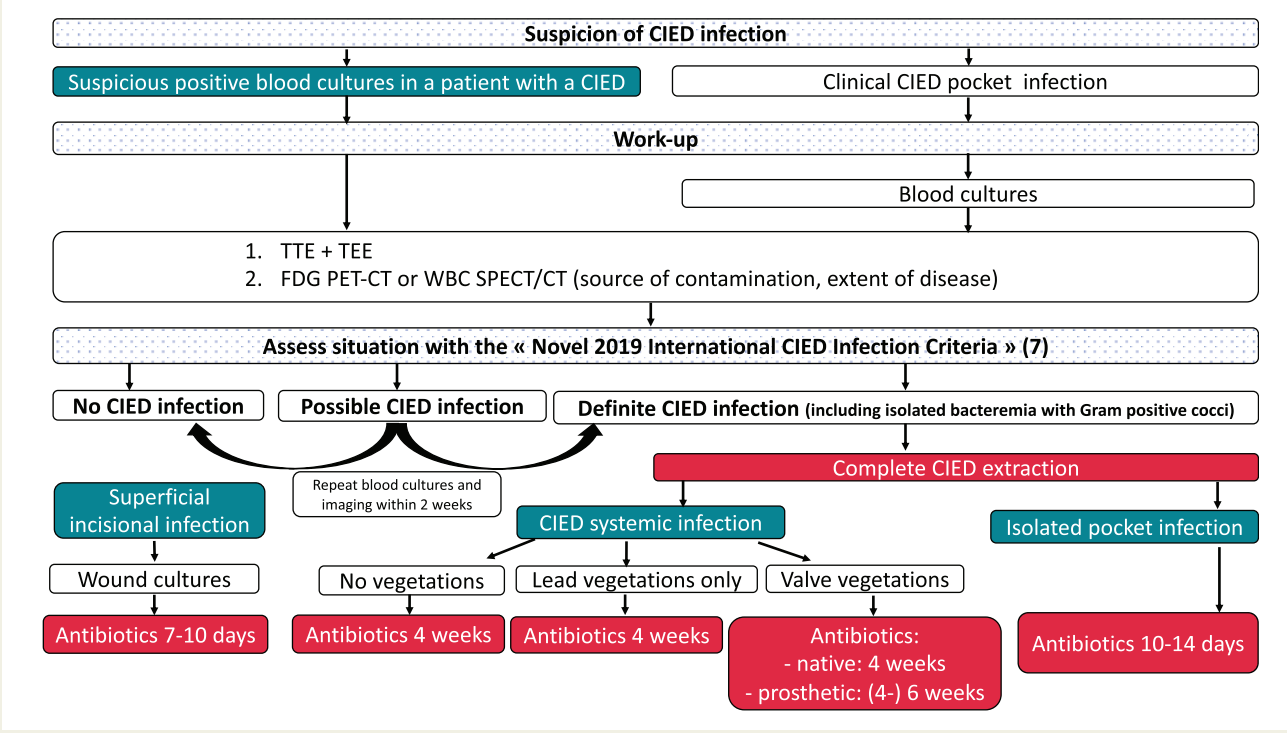

Figure 1 Proposed practical diagnosis and treatment (red) approach for the four clinical scenarios (green) of CIED infections. CIED, cardiac implantable electronic device; FDG PET-CT, fluorodeoxyglucose positron emission tomography—computed tomography; PV, prosthetic heart valve; TOE, transoesophageal echocardiography; TTE, transthoracic echocardiography; WBC SPECT/CT, white blood cell single-photon emission computed tomography—computed tomography.

oral antibiotic therapy covering *S. aureus* for 7–10 days. Importantly, close follow-up of the patient is mandatory to detect early extension of the infection to the pocket.[7]

Cardiac implantable electronic device pocket infection

A CIED pocket infection is defined as an infection of the generator pocket (*Figure 2A*). It manifests with local inflammatory changes, including pocket erythaema (41%), swelling (38%), pain and tenderness (28%), warmth (18%), drainage (38%), and/or device exposure (21%).[8,9] Once the generator and/or the proximal parts of the leads are exposed, the CIED system has to be considered infected irrespective of the Microbiological results, because it is in direct communication with the skin and its bacterial pathogens.[10] Pocket infection can be isolated or associated to systemic CIED infection.[8] The accumulation of bacteria and extracellular polymeric matrix constitute a biofilm, which protects the microbes from antibiotics and host defenses,[11] and helps the infection to track along the hardware to reach intravascular and intracardiac portions of the CIED system. In that view, vegetations were detected in 46% of patients presenting with clinical pocket infection in the cohort of Tarakji *et al.*[9] and Bongiorni *et al.*[12] reported that culture of the majority of their extracted electrodes (88.7%) resulted positive despite most of the patients (65.4%) had only local signs of infection. Therefore, blood cultures and transthoracic as well as transoesophageal echocardiography are recommended (statement class 'green') in all patients with clinical CIED pocket infection.

Cardiac implantable electronic device systemic infection

A CIED systemic infection is caused by infection of the intravascular parts of the device (*Figure 2B*). The diagnosis of CIED systemic infection without pocket infection is especially challenging and approximate the one of infective endocarditis. The symptoms are usually non-specific and include fever, chills, night sweats, and weight loss.[13] Addressing the need for more specific diagnostic criteria for patients implanted with CIED, the 'Novel 2019 International CIED Infection Criteria'[7] added specific CIED-related infection criteria to the 'ESC 2015 modified criteria for the diagnosis of infective endocarditis'.[13] In that view, clinical or radiological signs of pocket infection or lead vegetations are considered major criteria.[7]

More patients (58–65%) present with pocket infections rather than systemic CIED infection.[9,12,14] Although CIED infection within 6 months following device surgery seems to present more likely with pocket infection while late CIED infection are more often systemic, the timing of the infection after CIED procedure alone does not reliably suggest whether an infection is localized or systemic.[15]

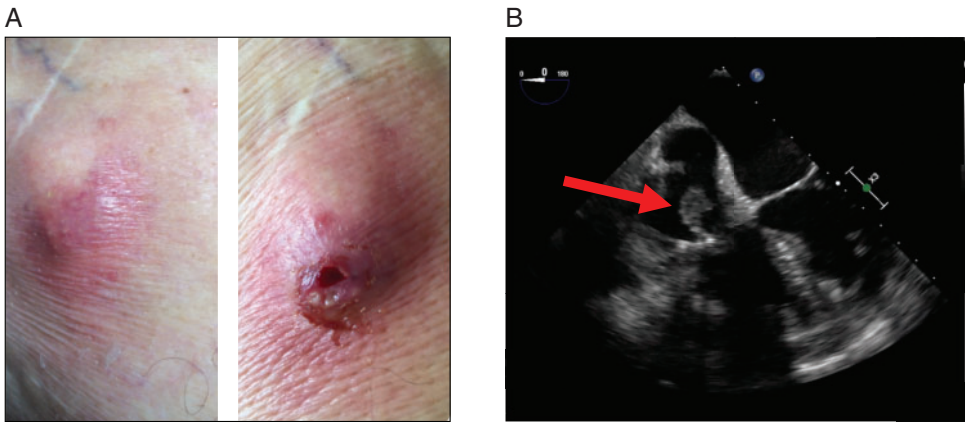

Figure 2 (*A*) Device pocket infection with perforation 1 week later. (*B*) Transoesophageal echocardiography showing a large vegetation attached to the tricuspidal valve and right ventricular lead.

Positive blood cultures in patients with cardiac implantable electronic device

Blood cultures are the first-line tool for the diagnosis of bloodstream infections. Their main weaknesses are the risk of contamination during sampling and false-negative results due to previous antibiotic therapy. The prevalence of blood culture contamination varies from 0.6% to 17%, explained by hospital-, staff- and patient-related factors, such as teaching-hospital labelling, workload of medical staff, and patients' comorbidities.[16] Patients undergoing CIED extraction because of infection are no exception, and the species isolated from blood cultures have been shown to often differ from those found on lead culture, being therefore rather likely the result of contamination.[12] The most important predictor of contamination is the identity of the microorganism isolated in blood culture, with *coagulase-negative Staphylococci* (CoNS), *Micrococcus* spp., viridans group streptococci, *Propionibacterium acnes* (*Cutibacterium acnes*), *Corynebacterium* spp., *Clostridium perfringens*, and *Bacillus* spp. being most often cited.[16] In that view, at least three sets of blood cultures should always be acquired before antibiotic therapy in case of clinically suspected CIED infection, and every effort should be made to perform clean samplings.[7]

Cardiac implantable electronic device infection is monomicrobial in the majority of cases. Consistent with our report,[17] CoNS were the most frequently isolated pathogens (69%) in consecutive patients ($n = 1204$) with infected PM or ICD who underwent transvenous removal in Pisa 2000–2011, followed by *S. aureus* (13.8%). Only 6.1% of CIED infections were caused by gram-negative bacilli and CIED fungal infection is uncommon, identified in only 1%.[12]

Although one single blood culture positive for CoNS provides insufficient evidence to dictate a therapeutic strategy in patients with CIED,[12] *S. aureus* should always be considered as pathogen, and evaluation for a source should be undertaken besides the workup of possible CIED infection.[8]

As shown in *Table 1*, the prevalence of CIED infection in patients presenting with positive blood cultures varies from 4% to 45% depending on the isolated pathogen. At least a transthoracic and transoesophageal echocardiography should be performed in bacteraemic patients with suspected CIED infection, with recommended repetition of the examinations within 5–7 days if clinical suspicion of CIED-related endocarditis remains high.[7] In the absence of signs of pocket or systemic CIED infection at initial presentation, the outcomes depend on the pathogen isolated in blood cultures. The reported rates of CIED infection in patients presenting with *S. aureus* bacteraemia range from 30% to 75% depending on definition and time delay from implantation.[18,19,22] In the report of Chamis *et al.*,[19] CIED infection was confirmed at initial evaluation in 15/33 (45.5%) CIED patients suffering from *S. aureus* bacteraemia, and 9/18 (50%) of the remaining patients initially without evidence of CIED infection and no device extraction presented a recurrent infection within 12 weeks and/or evidence of CIED infection at autopsy.[19] On the other hand, among the 74 consecutive CIED patients with bacteraemia caused by gram-positive cocci other than *S. aureus* who presented to Mayo Clinic between 2001 and 2007, 22 (29.7%) had a confirmed CIED infection at initial evaluation. *Coagulase-negative staphylococci* accounted for 73% of those. Relapse of bacteriaemia within 12 weeks of completion of antibiotic therapy occurred in 5/16 (31.3%) patients with CoNS bacteraermia without initial evidence of CIED infection, without device extraction, and who survived to discharge. No case of relapse was reported in patients with *non-staphylococcal gram-positive cocci* without initial definite CIED infection.[20] Finally, in sharp contrast to bacteraemia with gram-positive cocci, Uslan *et al.* reported a diagnosis of definite CIED endocarditis in only 2/49 (4.1%) patients with gram-negative bacteraemia. Both patients had an obvious pocket infection at presentation. Among the 34 patients who did not undergo system removal and survived >12 weeks only 2 (5.8%) developed relapsing bacteraemia (caused by *Klebsiella pneumoniae* in both), most likely explained by the clinical alternative sources of relapse.[21] Theses differences are most likely due to the variable ability of the bacteria to produce biofilm, helping them to evade the innate and acquired host immune defence systems.[23]

Highlighting the need for aggressive management of staphylococcal CIED infections, Le *et al.*[23] reports an overall 1-year mortality of 16%

Table 1 Prevalence of intracardiac electronic device infection at initial evaluation and outcomes according to type of pathogen in CIED patients with bacteraemia

	Population	Definition of positive blood culture for inclusion	Definitions of CIED infection	Prevalence of intracardiac electronic device infection at initial evaluation and main outcomes
S. aureus[18]	131 consecutive CIED patients presenting at Mayo Clinic Rochester 2001–2011 with *S. aureus* bacteraemia and no clinical evidence of pocket infection.	Any positive blood culture.	'Definite CIED infection': vegetations on echocardiography, fulfilment of modified Duke criteria for 'definitive endocarditis', or positive cultures from the generator pocket or leads.	Definite CIED infection: 45/131 (34.3%) • Vegetations in 41/45 (91.1%) patients
S. aureus[19]	33 consecutive CIED patients presenting to Duke University Medical Center 1994–2000 with *S. aureus* bacteraemia.	>1 blood culture positive for *S. aureus*, or a single blood culture positive for *S. aureus* in a patient with clinical evidence of infection.	'Confirmed CIED infection': vegetations on echocardiography, fulfilment of the Duke criteria or positive cultures from the generator pocket or leads. 'Rejected CIED infection': no evidence of CIED infection at time of blood culture, no CIED extraction, no recurrent infection within 12 weeks, no evidence of CIED infection at autopsy. 'Possible CIED infection': death before confirmation or rejection.	Confirmed CIED infection: 15/33 (45.5%), clinically 3/15, and microbiologically 12/15. Possible + confirmed CIED infection: 24/33 (72.7%) Rejected CIED infection: 9/33 (27.3%) Mortality at 12 weeks: 10/21 (47.6%) patients without vs. 2/12 (16.7%) patients with CIED extraction, $P = 0.13$
CoNS[20]	44 consecutive CIED patients presenting to Mayo Clinic Rochester 2001–2007 with CoNS bacteraemia.	Any non-contaminated blood culture from a peripheral blood sample. Blood cultures were considered to be contaminated and excluded if CoNS, *Micrococcus* species, *enterococci*, or viridans group *streptococci* were identified in only 1 set of culture.	'Definite CIED infection ': clinical pocket infection, vegetations on echocardiography, fulfilment of the modified Duke criteria or positive cultures from the generator pocket or leads.	Definite CIED infection: 16/44 (36.4%) • Vegetations in 10/16 (62.5%) patients Relapse at 12 weeks: 5/16 (31.3%) patients without initial CIED infection, no CIED extraction, no in-hospital death, and no lost to follow-up.
Non-Staphylococcal gram-positive coccus bacteraemia[20]	30 consecutive patients presenting to Mayo Clinic Rochester 2001–2007 with non-staphylococcal gram-positive coccus bacteraemia.			Definite CIED infection: 6/30 (20.0%) • Vegetations in 5/6 (83.3%) patients Relapse at 12 weeks: 0/16 (0.0%) patients without initial CIED infection, no CIED extraction, no in-hospital death, and no lost to follow-up.
Gram-negative bacteraemia[21]	49 consecutive patients hospitalized at Mayo Clinic Rochester 1998–2005 with gram-negative bacteraemia.	Any blood culture from a peripheral sample.	'Definite CIED infection': clinical pocket infection, presence of vegetations on echocardiography, or fulfilment of Duke criteria, or positive culture from the generator pocket or lead(s). 'Rejected CIED infection': no evidence of CIED infection at the time of initial blood culture, no CIED extraction, and no relapse of infection during a 12-week follow-up period.	Definite CIED infection: 2/49 (4.1%) • 2/2 (100.0%) patients with clinical pocket infection • 0/49 (0.0%) patients with systemic CIED infection Rejected CIED infection: 34/49 (69.4%) Relapse at 12 weeks: 2/34 (6%) patients without initial evidence of CIED infection, no CIED extraction, and no death. • 2/2 (100.0%) clear alternative source of relapse other than CIED and no evidence of CIED infection at time of relapse.

CIED, cardiac implantable electronic device; CoNS, coagulase-negative *Staphylococci*.

Table 2 Recommended[7,8,25] empirical antibiotic therapy regimens until identification of the microbiological aetiology according to the clinical scenarios (patients with normal renal function)

Clinical scenario	Recommended empirical antibiotic therapy regimens[7,8,25]
Superficial incisional infection	Flucloxacillin p.o. 1 g every 6–8 h *If high MRSA prevalence or penicillin-allergy*: clindamycine p.o. 450 mg every 6 h, doxycyclin p.o. 100 mg every 12 h, and linezolid p.o. 600 mg every 12 h
Isolated CIED pocket infection	Vancomycin i.v. 30–60 mg/kg/day in 2–3 doses *Alternative*: daptomycin i.v. 8–10 mg/kg every 24 h *If systemic symptoms*: add ceftriaxone i.v. 2 g every 24 h (or a broader betalactam antibiotic) OR gentamycin i.v. 5–7 mg/kg every 24 h
CIED systemic infection (including suspicious positive blood cultures in a patient with a CIED)	Vancomycin i.v. 30–60 mg/kg/day in 2–3 doses *Alternative*: daptomycin i.v. 8–10 mg/kg every 24 h AND Ceftriaxone i.v. 2 g every 24 h (or a broader betalactam antibiotic) OR gentamycin i.v. 5–7 mg/kg every 24 h *If staphylococcal prosthetic valve infection*: add rifampicin p.o. or i.v. 900–1200 mg/day in 2 doses after 5–7 days

CIED, cardiac implantable electronic device; i.v., intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*; p.o., per oral.

(late S. *aureus* infection 36%, CoNS 11%, $P < 0.001$). In comparison, non-staphylococcal CIED infection is far less virulent, with a reported need for intensive care admission in only 8% of patients and an overall mortality of 4%.[24]

Based on those results, complete CIED removal is indicated in bacteraemia or fungaemia with *S. aureus, coagulase-negative Staphyloccoci, Cutibacterium* spp., and *Candida* spp., whereas in bacteraemia with alpha- or beta-haemolytic *Streptococcus* spp. and *Enterococcus* spp. a complete CIED removal may be performed as first-line treatment or postponed in the case of recurrent/continued bacteraemia despite appropriate antibiotic therapy. In case of bacteraemia with non-pseudomonal/Serratia gram-negative bacteria or *Pneumococcus* spp., CIED removal should only be performed in the case of recurrent/continued bacteraemia despite appropriate antibiotic therapy when there is no other identifiable source.[7]

Treatment of cardiac implantable electronic device infection

Antibiotic therapy is the first pillar in CIED infection management. It should be started promptly following blood culture sampling, and follow the principles of treatment of infectious endocarditis. *Table 2* summarizes the recommended empiric antibiotic therapy regimens until identification of the microbiological aetiology according to the clinical scenarios. Once the pathogen is identified (usually within 48 h), the antibiotic treatment has to be tailored to the antimicrobial susceptibility pattern.[13] The collaboration between cardiologists and microbiologists with expertise in the field of CIED infection is of paramount importance concerning antibiotic therapy.[7,13] The duration of therapy depends on the presence or not of concomitant systemic infection and vary from 10 to 14 days in case of isolated pocket infection to typically 4–6 weeks in case of positive blood cultures, vegetations, and/or prosthetic valves (*Figure 1*). Two weeks of parenteral antimicrobial therapy after device extraction has been advocated by some experts in case of non-*S. aureus* systemic CIED infection without valvular involvement and adequate clinical improvement.[7,8] In the absence of systemic CIED infection, switch to oral treatment after device removal is possible since the remaining infection only involves skin and soft tissue.[7] The day of lead extraction or first negative blood cultures (whichever occurred last) should be considered as reference for the calculation of therapy duration.[8]

Complete extraction of the infected CIED system and of any other device fragments, independently of their location, constitute the second pillar in CIED infection management.[7] Although the need for device extraction is obvious in case of lead vegetations or pocket infection, complete device and lead removal is also recommended for all patients with valvular endocarditis without definite involvement of the CIED system.[7,8] Complete CIED removal can be curative for patients with CIED infection even in the presence of prosthetic heart valves and thus helps to prevent repeated valve surgery.[8] Antimicrobial therapy without device removal was associated with a seven-fold increase in 30-day mortality in a retrospective review of all cases of CIED infections seen at Mayo Clinic Rochester between 1991 and 2008,[26] and CIED infection relapse has been described in 70% of patients with incomplete system removal.[27,28] Although patients suffering from systemic infection might need stabilization before the extraction procedure, there should be no unnecessary delay between diagnosis and device extraction, as immediate device removal was shown to be associated with a three-fold decrease in 1-year mortality [hazard ratio (HR) 0.35, 95% confidence interval (CI) 0.16–0.75].[26] On short-term, transvenous lead extraction within 3 days from admission has been correlated with shorter hospitalization and better survival.[29]

Percutaneous transvenous lead extraction is superior to surgical open extraction in terms of patients' safety and comfort,[30] and is recommended as first extraction strategy in most patients with transvenous CIED.[7] In the ELECTRA Registry (6493 leads with a median dwelling time 5.0 years, inter-quartile range 2.0–9.0; 34.9% dual coil ICD leads) complete lead extraction was achieved in 6212/6493 leads

(95.7%, 95% CI 95.2–96.2), thanks to the use of the several available tools (simple traction 27.3%, locking stylets 71.1%, mechanical non-powered sheaths 36.3%, mechanical dilator sheaths 7.7%, and laser sheaths 19.3%).[14] Due to the risk of procedure-related major complications (1.7%[14]), operators experience[31] as well as the immediate availability of back-up heart surgery is of paramount importance.[8]

Although in case of large-sized vegetations (>1 cm) open surgical extraction has been suggested by some authors[13,32] to minimize risk of embolism,[33] Meier-Ewert *et al.* demonstrated the safety of percutaneous extraction even in the presence of large vegetations on endocardial leads (10–38 mm). All of their patients underwent successful device removal and all of the 5/9 patients with secondary pulmonary embolism made a full recovery with antibiotic treatment and anticoagulation.[34] Percutaneous vegetation aspiration has recently been shown to be safe and highly successful (>90%) in complete removal of all vegetative material as determined by transoesophageal echocardiography.[35] As there is some evidence in favour of an increase in mortality as a function of vegetation size,[36] this technique could become increasingly used to reduce the risk of septic embolism and infectious material bulk in patients with lead vegetations. In line with our report of a PM lead vegetation trapped in a patent foramen oval (PFO) causing hypoxemia after percutaneous lead extraction,[37] Lee *et al.*[38] reported an overall stroke rate of 1.9% during percutaneous lead extraction procedures, with PFO being independently associated with stroke occurrence, especially in the presence of right-sided vegetations and right-to-left shunt. Therefore, surgical CIED extraction may be considered in case of large vegetation size,[7] particularly in the context of right-to-left shunt without available percutaneous vegetation aspiration. Obviously, surgery should be the preferred technique when a combined surgical treatment (e.g. valve repair or replacement) is indicated.

Chronic antibiotic suppression has been proposed in case of refusal of the extraction or comorbidities precluding the intervention. Tan *et al.*[39] report a median survival of only 1.43 years (95% CI 0.27–2.14) with chronic antibiotic suppression, with 18% of their patients suffering an infection relapse within 1 year. Finally, some authors have described successful treatment, at least on short-term, of isolated pocket infection with surgical debridement, negative pressure, and/or closed irrigation systems with antibiotics. However, these almost palliative procedures have to be reserved for very selected patients who are too frail or sick to undergo lead extraction.[40]

While there are many similarities in the management of CIED infection whether it presents as pocket infection or systemic infection, the overall prognosis of these two types of presentation is different, with a significantly higher overall mortality (OR 4.93, 95% CI 2.72–8.93, $P < 0.0001$) in case of systemic infection.[14] This difference remains not completely explained, and might results from differences in decisions concerning reimplantation, duration of antibiotic therapy, and comorbidities.

Device reimplantation and outcomes

The indication, approach, and timing for device reimplantation are often challenging.[41] Obviously, no part of the removed CIED should be reused.

First, the indication for reimplantation should be thoroughly reevaluated following complete CIED system extraction. Some patients might have had improvement in rhythm or cardiac function and no longer meet a guideline indication for permanent PM, ICD, or resynchronization therapy, while others might not wish to receive a new device.[8] In that view, reported reimplantation rates vary from 58% to 86%.[27,42,43]

Secondly, the replacement device should be implanted at a different anatomical site with use of an alternative lead access such as the contralateral subclavian vein, an iliac vein, or by surgical epicardial lead placement.[11,44]

Finally, the reimplantation should be deferred until signs and symptoms of local and systemic infection have resolved, and postponed to allow blood culture to remain negative during 48–72 h.[7] A delay of 14 days has been proposed in case of valve vegetations.[7,11] Tarakji *et al.*[9] reported an increased risk of infection relapse at one year in patients implanted during the same hospitalization as hardware removal (2.6% vs. 1.9% for the overall cohort). This finding stresses the importance of a sufficient waiting period before safe device reimplantation. Obviously, such a delay is especially challenging in pacing-dependent patients. Due to the inerrant risks of lead displacement or ventricular perforation, and to avoid complications resulting from immobilization, passive fixation temporary PM leads are not recommended for bridging the stimulation.[13,27] Instead, the implantation of an epicardial device before extraction, or the use of an ipsilateral screwed-in provisory PM lead with a view to definitive delayed endocardial reimplantation, have been proposed as alternatives in those patients (*Figure 3*). In our retrospective single-centre study including two cohorts of consecutive PM-dependent patients who underwent transvenous lead extraction at our tertiary hospital, we found no difference in long-term mortality between epicardial device reimplantation before extraction or bridging stimulation with a screwed-in provisory PM lead. The strategy of provisory pacing was associated with a significantly reduced risk of late endocarditis and device reintervention (HR 0.25, 95% CI 0.09–0.069, $P = 0.01$). In facts, ~25% of our patients with an epicardial CIED required reimplantation of an endocardial device, mainly for cardiac resynchronization or antitachycardia protection. Based on those finding, epicardial CIED reimplantation should be primarily reserved for patients needing anyways heart surgery. That be, stressing the difficulty of infect control in systemic CIED infection, 25% of our patients with a provisory screwed-in pacing wire were finally reimplanted epicardially, mainly because of infection of their provisory lead despite guideline-conform antibiotic therapy.[45] In case of epicardial reimplantation, every efforts should be made to immediately implant the most suited device according to the clinical condition, to avoid future reinterventions. In consequence to the reported increased risk of epicardial lead fracture,[46] we consider in particular situations the implantation of a second ventricular epicardial lead, which we leave caped in the abdominal device pocket. In case of a lead issue during follow-up, only a pocket revision with connection of the backup lead is needed in those patients.

New kinds of CIED have been designed recently to reduce the amount of intravascular material or suppress it completely. A single-chamber ventricular PM can be implanted trough femoral venous access directly into the right ventricle.[47] Also, a completely extra-thoracic subcutaneous defibrillator system is available for patients having an indication for ICD implantation but no need for pacing or

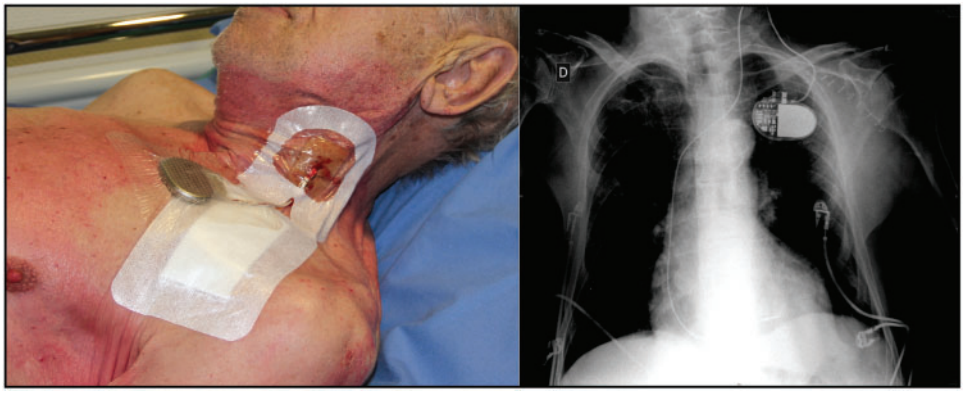

Figure 3 'Semi-permanent' provisory pacing for bridging of cardiac stimulation following complete CIED extraction on the left side. A reuse pacemaker generator is strapped on patient's skin and connected to a conventional right ventricular screw-in lead introduced through the ipsilateral jugular vein. This provisory material will be removed immediately after delayed contralateral reimplantation. CIED, cardiac implantable electronic device.

cardiac resynchronization therapy. Making those devices especially interesting following CIED extraction due to infection, all serious infectious events (endocarditis or bacteraemia) in the investigational device exemption study of the leadless PM could be treated successfully with antibiotics,[48] and the consequences of systemic infection are obviously lessened by the absence of endovascular material in patients with extra-thoracic subcutaneous ICD.

Conclusion

Cardiac implantable electronic device infection remains a major matter of concerns in cardiology. In-hospital mortality is impressive (4.11%)[49] and worsened long-term prognosis has been suggested.[50] Every effort must be made to ensure that care providers have good knowledge of the different clinical scenarios of CIED infection and offer guideline-conform management to affected patients. Reassuringly, patients treated according to guidelines in the present era seem to have similar prognosis to CIED patients without device infection.[17,51] That be, the main focus in management of CIED infection should obviously remain the prevention of its occurrence.

Funding

This article was published as part of a supplement supported by an educational grant from Medtronic.

Conflict of interest: none declared.

References

1. Raatikainen MJP, Arnar DO, Merkely B, Nielsen JC, Hindricks G, Heidbuchel H *et al.* A decade of information on the use of cardiac implantable electronic devices and interventional electrophysiological procedures in the European Society of Cardiology countries: 2017 report from the European Heart Rhythm Association. *Europace* 2017;**19**:ii1–90.
2. Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA *et al.* 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). *Europace* 2013;**15**:1070–118.
3. Brignole M, Moya A, de Lange FJ, Deharo JC, Elliott PM, Fanciulli A *et al.*; ESC Scientific Document Group. 2018 ESC Guidelines for the diagnosis and management of syncope. *Eur Heart J* 2018;**39**:1883–948.
4. Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J *et al.* 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. *Europace* 2015;**17**:1601–87.
5. Voigt A, Shalaby A, Saba S. Continued rise in rates of cardiovascular implantable electronic device infections in the United States: temporal trends and causative insights. *Pacing Clin Electrophysiol* 2010;**33**:414–9.
6. Olsen T, Jørgensen OD, Nielsen JC, Thøgersen AM, Philbert BT, Johansen JB. Incidence of device-related infection in 97 750 patients: clinical data from the complete Danish device-cohort (1982-2018). *Eur Heart J* 2019;**40**:1862–9.
7. 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). *Europace* 2020.
8. Kusumoto FM, Schoenfeld MH, Wilkoff BL, Berul CI, Birgersdotter-Green UM, Carrillo R *et al.* 2017 HRS expert consensus statement on cardiovascular implantable electronic device lead management and extraction. *Heart Rhythm* 2017;**14**:e503–51.
9. 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**:1043–7.
10. Tsai V, Chen H, Hsia H, Zei P, Wang P, Al-Ahmad A. Cardiac device infections complicated by erosion. *J Interv Card Electrophysiol* 2007;**19**:133–7.
11. Baddour LM, Epstein AE, Erickson CC, Knight BP, Levison ME, Lockhart PB *et al.*; Council on Cardiovascular Surgery and Anesthesia. Update on cardiovascular implantable electronic device infections and their management: a scientific statement from the American Heart Association. *Circulation* 2010;**121**:458–77.
12. Bongiorni MG, Tascini C, Tagliaferri E, Di Cori A, Soldati E, Leonildi A *et al.* Microbiology of cardiac implantable electronic device infections. *Europace* 2012;**14**:1334–9.
13. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F *et al.* 2015 ESC Guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015;**36**:3075–128.
14. Bongiorni MG, Kennergren C, Butter C, Deharo JC, Kutarski A, Rinaldi CA *et al.*; ELECTRa Investigators. The European Lead Extraction ConTRolled (ELECTRa) study: a European Heart Rhythm Association (EHRA) Registry of Transvenous Lead Extraction Outcomes. *Eur Heart J* 2017;**38**:2995–3005.
15. Sohail MR, Hussain S, Le KY, Dib C, Lohse CM, Friedman PA *et al.*; for the Mayo Cardiovascular Infections Study Group. Risk factors associated with early- versus

late-onset implantable cardioverter-defibrillator infections. *J Interv Card Electrophysiol* 2011;**31**:171–83.
16. Dargère S, Cormier H, Verdon R. Contaminants in blood cultures: importance, implications, interpretation and prevention. *Clin Microbiol Infect* 2018;**24**:964–9.
17. Deharo JC, Quatre A, Mancini J, Khairy P, Le Dolley Y, Casalta JP *et al.* Long-term outcomes following infection of cardiac implantable electronic devices: a prospective matched cohort study. *Heart* 2012;**98**:724–31.
18. Sohail MR, Palraj BR, Khalid S, Uslan DZ, Al-Saffar F, Friedman PA *et al.* Predicting risk of endovascular device infection in patients with *Staphylococcus aureus* bacteremia (PREDICT-SAB). *Circ Arrhythm Electrophysiol* 2015;**8**:137–44.
19. Chamis AL, Peterson GE, Cabell CH, Corey GR, Sorrentino RA, Greenfield RA *et al.* Staphylococcus aureus bacteremia in patients with permanent pacemakers or implantable cardioverter-defibrillators. *Circulation* 2001;**104**:1029–33.
20. Madhavan M, Sohail MR, Friedman PA, Hayes DL, Steckelberg JM, Wilson WR *et al.*; for the Mayo Cardiovascular Infections Study Group. Outcomes in patients with cardiovascular implantable electronic devices and bacteremia caused by Gram-positive cocci other than *Staphylococcus aureus*. *Circ Arrhythm Electrophysiol* 2010;**3**:639–45.
21. Uslan DZ, Sohail MR, Friedman PA, Hayes DL, Wilson WR, Steckelberg JM *et al.* Frequency of permanent pacemaker or implantable cardioverter-defibrillator infection in patients with gram-negative bacteremia. *Clin Infect Dis* 2006;**43**:731–6.
22. Uslan DZ, Sohail MR, St Sauver JL, Friedman PA, Hayes DL, Stoner SM *et al.* Permanent pacemaker and implantable cardioverter defibrillator infection: a population-based study. *Arch Intern Med* 2007;**167**:669–75.
23. Le KY, Sohail MR, Friedman PA, Uslan DZ, Cha SS, Hayes DL *et al.* Clinical features and outcomes of cardiovascular implantable electronic device infections due to staphylococcal species. *Am J Cardiol* 2012;**110**:1143–9.
24. Viola GM, Awan LL, Darouiche RO. Nonstaphylococcal infections of cardiac implantable electronic devices. *Circulation* 2010;**121**:2085–91.
25. Sandoe JA, Barlow G, Chambers JB, Gammage M, Guleri A, Howard P *et al.* Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a Joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHRS), British Cardiovascular Society (BCS), British Heart Valve Society (BHVS) and British Society for Echocardiography (BSE). *J Antimicrob Chemother* 2015;**70**:325–59.
26. Le KY, Sohail MR, Friedman PA, Uslan DZ, Cha SS, Hayes DL *et al.* Impact of timing of device removal on mortality in patients with cardiovascular implantable electronic device infections. *Heart Rhythm* 2011;**8**:1678–85.
27. Sohail MR, Uslan DZ, Khan AH, Friedman PA, Hayes DL, Wilson WR *et al.* Management and outcome of permanent pacemaker and implantable cardioverter-defibrillator infections. *J Am Coll Cardiol* 2007;**49**:1851–9.
28. Pichlmaier M, Knigina L, Kutschka I, Bara C, Oswald H, Klein G *et al.* Complete removal as a routine treatment for any cardiovascular implantable electronic device-associated infection. *J Thorac Cardiovasc Surg* 2011;**142**:1482–90.
29. Viganego F, O'Donoghue S, Eldadah Z, Shah MH, Rastogi M, Mazel JA *et al.* Effect of early diagnosis and treatment with percutaneous lead extraction on survival in patients with cardiac device infections. *Am J Cardiol* 2012;**109**:1466–71.
30. Rusanov A, Spotnitz HM. A 15-year experience with permanent pacemaker and defibrillator lead and patch extractions. *Ann Thorac Surg* 2010;**89**:44–50.
31. Deharo JC, Bongiorni MG, Rozkovec A, Bracke F, Defaye P, Fernandez-Lozano I, Authors (EHRA Task Force Members) *et al.* Pathways for training and accreditation for transvenous lead extraction: a European Heart Rhythm Association position paper. *Europace* 2012;**14**:124–34.
32. Camboni D, Wollmann CG, Löher A, Gradaus R, Scheld HH, Schmid C. Explantation of implantable defibrillator leads using open heart surgery or percutaneous techniques. *Ann Thorac Surg* 2008;**85**:50–5.
33. Mügge A, Daniel WG, Frank G, Lichtlen PR. Echocardiography in infective endocarditis: reassessment of prognostic implications of vegetation size determined by the transthoracic and the transesophageal approach. *J Am Coll Cardiol* 1989; **14**:631–8.
34. Meier-Ewert HK, Gray ME, John RM. Endocardial pacemaker or defibrillator leads with infected vegetations: a single-center experience and consequences of transvenous extraction. *Am Heart J* 2003;**146**:339–44.
35. Starck CT, Schaerf RHM, Breitenstein A, Najibi S, Conrad J, Berendt J *et al.* Transcatheter aspiration of large pacemaker and implantable cardioverter-defibrillator lead vegetations facilitating safe transvenous lead extraction. *Europace* 2020;**22**:133–8.
36. Greenspon AJ, Le KY, Prutkin JM, Sohail MR, Vikram HR, Baddour LM *et al.* Influence of vegetation size on the clinical presentation and outcome of lead-associated endocarditis: results from the MEDIC registry. *JACC Cardiovasc Imaging* 2014;**7**:541–9.
37. Le Dolley Y, Thuny F, Bastard E, Riberi A, Tafanelli L, Renard S *et al.* Images in cardiovasclar medicine: pacemaker lead vegetation trapped in patent foramen ovale: a cause of hypoxemia after percutaneous extraction. *Circulation* 2009;**119**: e223–4.
38. Lee JZ, Agasthi P, Pasha AK, Tarin C, Tseng AS, Diehl NN *et al.* Stroke in patients with cardiovascular implantable electronic device infection undergoing transvenous lead removal. *Heart Rhythm* 2018;**15**:1593–600.
39. Tan EM, DeSimone DC, Sohail MR, Baddour LM, Wilson WR, Steckelberg JM *et al.* Outcomes in patients with cardiovascular implantable electronic device infection managed with chronic antibiotic suppression. *Clin Infect Dis* 2017;**64**: 1516–21.
40. Glikson M. Conservative treatment of pacemaker pocket infection: is it a viable option? *Europace* 2013;**15**:474–5.
41. Gould PA, Gula LJ, Yee R, Skanes AC, Klein GJ, Krahn AD. Cardiovascular implantable electrophysiological device-related infections: a review. *Curr Opin Cardiol* 2011;**26**:6–11.
42. Al-Hijji MA, Killu AM, Yousefian O, Hodge DO, Park JY, Hebsur S *et al.* Outcomes of lead extraction without subsequent device reimplantation. *Europace* 2017;**19**:1527–34.
43. Boyle TA, Uslan DZ, Prutkin JM, Greenspon AJ, Baddour LM, Danik SB *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**. doi: 10.1161/CIRCEP.116.004822.
44. Amraoui S, Barandon L, Whinnett Z, Ploux S, Labrousse L, Denis A *et al.* Single surgical procedure combining epicardial pacemaker implantation and subsequent extraction of the infected pacing system for pacemaker-dependent patients. *J Thorac Cardiovasc Surg* 2013;**146**:302–5.
45. Perrin T, Maille B, Lemoine C, Resseguier N, Franceschi F, Koutbi L *et al.* Comparison of epicardial vs. endocardial reimplantation in pacemaker-dependent patients with device infection. *Europace* 2018;**20**:e42–50.
46. Papadopoulos N, Rouhollapour A, Kleine P, Moritz A, Bakhtiary F. Long-term follow-up after steroid-eluting epicardial pacemaker implantation in young children: a single centre experience. *Europace* 2010;**12**:540–3.
47. Reynolds D, Duray GZ, Omar R, Soejima K, Neuzil P, Zhang S *et al.* A leadless intracardiac transcatheter pacing system. *N Engl J Med* 2016;**374**:533–41.
48. El-Chami MF, Soejima K, Piccini JP, Reynolds D, Ritter P, Okabe T *et al.* Incidence and outcomes of systemic infections in patients with leadless pacemakers: data from the Micra IDE study. *Pacing Clin Electrophysiol* 2019;**42**:1105–10.
49. Hosseini SM, Rozen G, Kaadan MI, Galvin J, Ruskin JN. Safety and in-hospital outcomes of transvenous lead extraction for cardiac implantable device-related infections: analysis of 13 years of inpatient data in the United States. *JACC Clin Electrophysiol* 2019;**5**:1450–8.
50. Rizwan Sohail M, Henrikson CA, Jo Braid-Forbes M, Forbes KF, Lerner DJ. Increased long-term mortality in patients with cardiovascular implantable electronic device infections. *Pacing Clin Electrophysiol* 2015;**38**:231–9.
51. Rickard J, Tarakji K, Cheng A, Spragg D, Cantillon DJ, Martin DO *et al.* Survival of patients with biventricular devices after device infection, extraction, and reimplantation. *JACC Heart Fail* 2013;**1**:508–13.